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A SURGEON'S REFLECTIONS ON MEDICAL EDUCATION

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A DISTINCT honor has been conferred upon the Society of University Surgeons by the invitation to participate in this Centennial Celebration of the birth of William Stewart Halsted. Certainly nothing could have given me greater pleasure than to preside over this meeting here where I had my formal medical education, the first years of my training in surgery and in surgical research, and my initial experiences in teaching.

The shadow of Halsted looms large over the entire field of surgery. He developed a method of operative attack based upon careful attention to fundamental principles of tissue injury and repair, emphasizing gentle, nontraumatic dissection, exact hemostasis, and precise approximation of divided tissues. His original contributions from the wards, the operating rooms, and the experimental laboratory are among the greatest made by any physician throughout the entire period of medical history. No individual did more to encourage the development of the then infant surgical specialties—neurological surgery, urology, and otolaryngology. Perhaps the most far-reaching contribution of Professor Halsted, however, was his training of surgeons. Like him, they were so well grounded in the basic fundamentals, so wholeheartedly interested in the well-being of patients, so critical in judgment, so inquisitive and aflame with the desire to participate actively in advancing scientific knowledge, and so imbued with the challenge of teaching and of training young surgeons that they have gone to the far corners of the nation as heads of university departments. Indeed, at this time, Halsted's family tree—and this is particularly true if one considers not only his own progeny but those whom they in turn have developed—has branched until it has become the single most powerful force in university surgery. The system of residency training which he inaugurated, and which has been so widely followed, has stood the test of time. Without any fundamental

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change it has remained the finest method for developing young surgeons. Our Society has had as one of its principal objectives the extension and strengthening of such residency training programs.

Unfortunately, the teaching of surgery to medical students, and medical education in general, have not kept pace with the graduate training of surgeons. It may be profitable to review briefly some of the current deficiencies, to analyze the factors which seem responsible, and to propose certain avenues which might profitably be explored.

Progressively with the passage of years the teaching of medicine has become more and more complicated. The principal subjects which comprised the curriculum during Halsted's early days at Hopkins have all been broadened as new knowledge has been added and the scope of each has been extended. Think, for example, how much more difficult a problem the teaching of physiologic chemistry has become as the result of all the advances which have been made in that field. To mention only a few, the student must learn, in addition to all that physiologic chemistry formerly comprised, as much as is possible about the various enzyme reactions, acid base balance, the partition of body fluids and electrolytes, the vitamins, the hormones, and the metabolism of carbohydrates and lipids. One may take as a further example our own field. How much larger it has become with the extension of the realm of surgery into the central nervous system, the ears, nose, and oral cavity, the respiratory passages and lungs, the heart and great vessels; with the development of a firmer understanding of the basic physiopathologic processes which underlie the surgical disorders; and with the recognition of the everyday importance of the basic sciences in the management of surgical problems.

Not only has each of the principal medical disciplines been enlarged, but new ones have been added. Not many years ago the basic teaching of medicine could be conveniently grouped into anatomy, physiology, physiologic chemistry, pharmacology, pathology, medicine, obstetrics, pediatrics, psychiatry, and surgery. Surgery itself has given birth to ophthalmology, otolaryngology, orthopedics, urology, neurologic surgery, plastic surgery, thoracic surgery, vascular surgery, proctology, all of which have grown to such importance that they have been given departmental or sectional status in many institutions. As one glances through the medical school catalogues of 1952, one finds, in addition to the subjects which were formerly considered basic and the newer surgical specialties, the following subjects which are taught in separate courses and in many instances under separate departmental or sectional control: dermatology, preventive medicine, public health, cardiology, oncology, the history of medicine, clinical pathology, anesthesiology, radiology, legal or forensic medicine, physical medicine, industrial medicine, occupational medicine, dentistry, oral surgery, biophysics, gastroenterology, tropical medicine, military medicine, medical art, general practice, medical economics, and gerontology.

As each new aspect of the entire field of medicine has reached maturity, and not infrequently shortly after its birth, those interested in its development have demanded its inclusion in the curriculum. Unfortunately, seldom has it been proposed that this new teaching effort be incorporated into the other

medical disciplines but rather that it be inaugurated as an entirely new subject. Rare is it, for example, that those who are impressed with the new importance of problems of the aged suggest that they be emphasized on the medical, surgical, neurologic, orthopedic, and psychiatric wards and in the clinics. On the contrary, they are prone to insist that the subject be introduced into the curriculum as an independent course in geriatrics. Those who are imbued with the importance of physical medicine are not likely to suggest that its teaching be strengthened upon the wards and in the clinics but instead through new courses and by means of a new teaching unit.

Thus, the curriculum has become increasingly crowded with the expansion of old courses and the creation of entirely new ones. This crowding of the curriculum is not, however, the sole, or even perhaps the principal, problem created by the growth of medicine in general and the medical specialties in particular. More important is the fact that there has been a general tendency to neglect welding together all of this diverse subject matter, correlating it, and giving it proper balance. All too often each group in the medical faculty works alone and in its teaching effort emphasizes the importance of its own special interest rather than fitting it properly into the total effort.

As a result, the student faces, from the first day of medical school to the last, a bewildering mass of material which he tries frantically to grasp and store away, often as unrelated fragmentary bits of information. During his first two years he races from one basic science course to another, and toward the end of this period is briefly subjected to the methods of laboratory study and problems of history-taking and physical diagnosis. He then plunges into an equally harassing maze of clinical material, trying desperately to acquire as much knowledge as he can about the fundamental medical disciplines and the various medical specialties. In gross anatomy he learns the morphology of the kidney, its relationship to other organs, its blood and nerve supply. In an entirely separate course he studies its normal histology. On another occasion he seeks to learn something about its function. In a wholly different effort he is taught the action of drugs upon renal function. Subsequently, he acquires some knowledge of microbiology but his new knowledge is apt to come to him unrelated to the specific problem of infections of the kidney and the urinary excretory apparatus. He then learns something about the pathologic processes which affect the genitourinary system, generally from lifeless, fixed material. During all this time he is carefully guarded from contact with the human patient. He now becomes introduced to the methods used clinically in examining the urine and, briefly, to the methods of assessing renal function. He learns a bit about physical diagnosis and then he is confronted with the perplexing problems of the ill patient. In medicine he sees patients with nephritis, pyelitis, cystitis, and hypertension of nephrogenic origin. On the medical wards and in the ophthalmologic clinics he observes the effects of renal malfunction upon the retina. In medicine, neurologic surgery, and neurology he becomes acquainted with the cerebrovascular complications of hypertension. He is presented with its cardiologic manifestations. In obstetrics he deals with the toxemias of pregnancy. In surgery he learns the importance of urogenital infections and

tumors in the differential diagnosis of intra-abdominal inflammatory and neoplastic conditions. In pediatrics he is confronted with the genitourinary problems of childhood and, finally, in urology, he is acquainted with the whole gamut of neoplastic, infectious, and congenital conditions of the genitourinary system and learns something about the more precise methods of study of the urogenital tract. The same general sequence of events pertains to almost every organ and system of the human body and to almost all of the pathologic processes and physiologic disturbances which affect it. To be sure, the method is not without its virtues, but all too often it results in disunity rather than harmony, in the acquisition of undigested facts rather than basic principles. The student is all too apt to acquire knowledge rather than wisdom.

The crowded and confused state of the medical curriculum is entirely understandable. By and large, the faculty of the medical school is so busily engaged with the performance of its duties that it has little time to pause and analyze the organization and the results of its teaching effort. Its time is fully occupied with teaching, research, practice, administrative duties, committee meetings. As each member of the faculty reaches maturity and gains in stature, he is apt to have thrust upon him many other obligations which, though of great importance, are time consuming. He is likely to spend more and more time with matters concerning the various specialty societies. He may be asked to serve upon national examining boards. He may become a member of one or more national advisory committees. He must be concerned with a thousand and one things which changing times have brought intimately into the total problem of medical education: the cost of medical care and of medical education itself, the struggle for adequate financial support for hospitals and medical schools, the impact of the altered socioeconomic status and the growth of insurance upon the ward service which has constituted the traditional backbone of clinical instruction. He has little time left to contemplate the effectiveness of the teaching job which he is doing and its correlation with the total teaching effort.

I would be the last to infer that the system in vogue is turning out inferior doctors, and I would be the first to claim that the current products of medical education are performing their duties well and carrying on in an admirable fashion the many diverse obligations which fall to their lot. It seems to me, however, that it would be a tragic mistake to rest upon our oars in self-satisfied complacency. We cannot content ourselves with any ideal short of doing the very best job possible with the material at hand. In order to do so I believe that it will be necessary to consider radical alterations of the entire medical curriculum.

First, let us consider in a general way what our objectives are. It is our principal objective to train men who not only look and act like doctors, but who think like rational scientific men of medicine. We do not indulge in the futile hope of filling each student with such a mass of medical knowledge that it will suffice him forever. We desire rather to impart to him basic concepts and principles, to teach him methods for continuing all the days of his life his process of medical growth and maturation. We want him well grounded in the history of medicine, believing firmly that only he who understands clearly

past developments can face the present squarely and the future with both daring and caution. We do not aspire to unquestioned obeisance to authority. Rather we would cultivate in him respectful doubt and undying inquisitiveness. We would teach him to give free range to all his creative genius and, at the same time, the necessary virtue of control. He must recognize from first to last that we are called upon to treat, in the broadest sense of the word, the ill patient rather than his disease. We want to encourage his compassion for the sick, his appreciation for the thousand and one problems faced by the sick and dying and by their families, and if we fail in this regard, it is our duty to steer him into some sphere of work where he will have no contact with them. To this end it is of fundamental importance that the clinical faculty of the medical school be composed of individuals who carry out in the best tradition the ideal practice of medicine, exemplifying not only discriminating analysis, critical judgment, reason, and pliability, but sympathetic understanding as well.

In each of the medical disciplines it should be our primary aim to teach its importance as a part of the whole, to give the student a comprehension of its scope, its problems, its potentialities, and its limitations. It is not our desire, for example, to make each student a surgeon. It is our desire to give each student the basic principles which underlie surgery, to make him aware of its interrelationships with all the medical sciences and medicine in general. We want him to be fully cognizant of those disturbances which this field comprises, to understand their physiopathologic basis, to appreciate their danger, to know how they can be recognized and what can be done for them. To be sure, we have a right to hope that some of them will follow in our footsteps and it is our duty to inspire them to the best of our ability, but we must never forget that our principal objective is to turn out well-rounded students of medicine, not surgeons. The latter is the objective of our graduate training program.

I am impressed with the fundamental importance of centering our efforts upon the patient. Confronted with all the diverse facts and concepts which comprise medical knowledge, the student encounters great difficulty in retaining and assimilating them unless he has some peg upon which they may hang. The most useful peg is the patient himself. What the student learns in relationship to any given patient he tends to retain. Whenever it is found necessary to utilize animal experimentation in teaching, it should be carried out with the explicit objective of pointing out to the student either the similarity or dissimilarity of the response to that which characterizes the human being. I am equally convinced that the student should grow up in an atmosphere of investigation. It is not our sole objective to turn out practicing physicians and surgeons. It is equally our responsibility to train teachers and investigators, in the basic sciences as well as in the clinical field. Consequently, it is important that the faculties of medical schools comprise forward-looking men who are themselves taking an active part in the advancement of scientific knowledge. This aim, however, constitutes only one of the justifications for the belief that it is an absolute necessity that the student should be nourished in an investigative air. More important still is the fact that it provides the fertile soil in which are most likely to grow those assets which are so invaluable in the best practice of

medicine—a restless striving to do a better job, the capacity to weigh a matter with objectivity and come up with a valid solution, the relentless search for truth. Not only do we wish to give our students the best possible medical education, but we also want them to be cultured individuals with the broad background which will give them the basis for the personal happiness they deserve and the position of leadership in the community which will be their lot.

How are we to accomplish these objectives in the best possible manner? I think much can be gained by abandoning the rigid departmental teaching now in vogue and substituting a correlated program centered around the various body systems. The following program is suggested not as a final answer but as one valid basis for such a reorganization. The teaching effort in the medical school would be divided into two sections: the first dealing essentially with the fundamental principles and concepts which are to be gained from the basic sciences and the second with the application of these concepts and principles to the patient himself. During the initial period covering the first two years in the medical school the students would be divided into eight sections. Each student would spend three months in each of these sections, which would be constituted as follows:

1. *Neuropsychiatric Problems.*—To include the human personality, psychobiology, the brain, spinal cord, and peripheral nerves, the autonomic nervous system and the striated muscles.

2. *The Cardiovascular-Renal-Respiratory Systems.*

3. *Problems of Growth, Development, and Aging.*—To include a general survey of embryology, growth, maturation and aging of cells as well as of the body as a whole, the endocrine glands, especially as they influence growth, the osseous system, and the problem of neoplasia.

4. *Gastrointestinal, Metabolic, and Nutritional Problems.*—To include the gastrointestinal tract, the liver, biliary passages and pancreas, the glands of internal secretion affecting metabolic processes, and psychic and autonomic nervous influences upon the gastrointestinal and related organs.

5. *The Infectious Diseases.*—To include bacteriology, virology, immunology, parasitology, the antibiotic and chemotherapeutic agents, the physiopathology of infection, the principles of asepsis, the spleen, lymph nodes, and reticuloendothelial system, and hematologic problems not specifically covered in other sectional programs.

6, 7, and 8. *Elective and Vacation Periods.*

In each section all promising teaching aids would be utilized. There would be laboratory exercises and demonstrations, conferences, seminars, and patient demonstrations. Adequate time would be left for reading and for reflection. Whenever possible the student would learn from the human being rather than from the laboratory animal. The teaching staff would be selected from those especially interested in that particular problem. It would include clinicians, as well as those in the basic sciences upon whom the major teaching burden would rest. Everything would be done to help the student correlate his new knowledge and concepts, to give him motivation, enthusiasm, and balance. In

each section an effort would be made to begin with the simpler aspects of the problem. Consideration of normal structure and function would precede the abnormal. Patients would be utilized, not in an effort to teach clinical medicine in these early years, but to illustrate normal and abnormal structure and function, to give the study program rationale and cohesiveness, and to provide living evidence of the importance of basic concepts and principles in understanding the function and dysfunction of the human being.

As a result of these two years of study, the student should be well grounded in fundamentals and adequately prepared for beginning his clinical years. He should know not less, but more, of anatomy, physiology, pharmacology, physiologic chemistry, bacteriology, and pathology than he does after a similar period under the current regimen. In addition, what he has learned should be better correlated and integrated. Furthermore, he should have learned it more easily, more pleasantly, and with less wasted expenditure of time and energy.

The same sort of correlated, cooperative teaching should continue throughout the final years, though necessarily to a lesser degree as a result of the natural linkage of clinical teaching to the existent departmentalized plan for patient care. The basis for teaching would be the clinical clerkship augmented by appropriate conferences and clinics. During each clerkship the student would serve, as is customary in many institutions at the present time, as an integral part of the house staff team, performing the duties and sharing the learning opportunities of a junior intern. It is my conviction that the best organization links each student to a member of the resident staff with whom he works continuously and from whom he learns day and night. He takes part in all the house staff rounds and conferences.

We must never lose sight of the fact that the resident staff constitutes one of the most important segments of the faculty. The professor is the student's occasional instructor, the house staff his constant tutor. The able resident is fully aware of his obligation to help the student learn all he can of the fundamental physiologic and pathologic alterations which affect his patients, the rational methods of investigating and understanding these aberrations, and the broad principles which underlie their correction. He is just as cognizant as is the senior faculty that the student is not serving his clerkship in order to master the intricacies of specialized treatment and techniques. When Halsted inaugurated his residency system of training surgeons, he made a cardinal contribution to general medical education itself.

I am persuaded that it would be wise to abandon the widely prevalent policy of separating the final years of medical instruction into two phases consisting essentially of outpatient and inpatient activities. Instead, the ward services and the respective outpatient clinics would be the simultaneous responsibility of students and house staff. Because of the fact that at the beginning of any clerkship a certain amount of time must be spent in becoming familiar with the physical layout, with administrative problems, and with customary procedures followed in reference to patient care, causing necessary temporary dislocation of the student from his primary learning activities, it is suggested that the clerkship be relatively long and unbroken by abrupt changes from one serv-

ice to another. It might be an effective plan to have the student spend half his time on a medical, and half on a surgical, clerkship, leaving free only sufficient intervals for elective work and a brief vacation period. It would matter little whether the third year were predominantly medical and the fourth year predominantly surgical, or vice versa. Perhaps, because medicine is a more general and surgery a more specialized field, it might be preferable to have the third year devoted primarily to the former, the fourth year to the latter. An appropriate amount of time during the medical clerkship would be made available for neuropsychiatry and pediatrics and during the surgical clerkship for obstetrics and special fields of surgery.

How does the specialist fit into this scheme of things? It is apparent that there is no place in the curriculum for detailed presentation of the intricacies of any specialty. We cannot resurrect the long lectures in special fields recounting the minutiae of its particular diagnostic methods and outlining step by step the various operative procedures. It is equally apparent, however, that the well-rounded specialist should be just as able as the general physician or surgeon to orient his teaching along general lines. With proper balance he can contribute much to the student's basic understanding and to his grasp of the importance of careful history-taking, physical and laboratory diagnostic methods. The patient with a brain tumor or ureteral obstruction affords just as fine an opportunity for broadening the student's comprehension of basic principles as does the patient with intestinal obstruction or cardiac decompensation. Consequently, with proper direction of teaching efforts, the surgical clerks can gain invaluable experience on the surgical specialty wards.

During these final years every effort would be made to continue the cooperative teaching which characterized instruction in the first years. Participation in departmental rounds and conferences by members of other departments, preclinical as well as clinical, would be encouraged. In addition to the customary weekly student clinics in medicine and surgery, cooperative clinics and conferences relating to disorders of the various body systems would be held. During the medical clerkship there could be arranged, in addition, clinics and demonstrations dealing with special problems in medicine, psychiatry, pediatrics, and public health. Similarly, during the surgical clerkship there should be ample time for rounds and clinics devoted to problems falling into the sphere of obstetrics and special branches of surgery. All teaching would be centered about the patient. Dry clinics, lectures, and quiz sections would be abandoned.

It is to be noted that provision has not been made for inclusion of many subjects which have hitherto been presented as formal independent courses of instruction. This is done not with the intent that any basic material included in them should be omitted, but rather because of the belief that it can be presented more effectively in conjunction with the broader problems of medicine. I know of no finer way to teach surgical pathology than by the intelligent presentation to the student assistant in the operating room of the fresh pathologic material encountered at a time when he is steeped in the physiologic dysfunction it has brought about in his patient, and by demonstration and study week after week and month after month of the current surgical pathologic material

removed at operation. Numerous departments of radiology have shown without question what a superb job can be done, not through formally organized courses, but through weekly conferences held in conjunction with various departments and sections.

Such a revised curriculum could best be managed if some administrative reorganization took place. The existence of numerous equal and autonomous departments is not conducive to the cooperative effort necessary. Much could be said for organization of the entire faculty into three major departments or divisions, the basic sciences, medicine, and surgery. Subdivision of these major groups into appropriate smaller sections or departments would, of course, be necessary.

To me it would seem apparent that the sort of teaching program which I have outlined briefly would bear abundant fruit. It is only fair, however, to analyze its possible deficiencies. First, the question naturally arises whether a program of this kind would not require more teachers, laboratories, conference and classrooms, and clinical facilities. I believe this question would have to be answered in the affirmative and its implications constitute, therefore, a definite challenge in this era of handicapped financial structure, building needs, and limited clinical facilities. We cannot compromise on such grounds, however, the excellence of preparation of the physicians upon whom the national health depends. These problems will have to be met by aggressive action. Second, those in the basic sciences may justly ask whether this reorientation of the curriculum will deprive them of the opportunity to interest students in careers in these disciplines and whether it will forcibly direct their research along more practical clinical lines. Similarly, those in special fields of medicine and surgery may wonder whether the independent development of their own specialties will suffer as a consequence of being drawn back into the major mother departments. Such fears would seem groundless. Just as it is essential that all groups should work harmoniously together in the teaching effort in one common purpose, so is it mandatory that each unit have complete freedom and every aid in its growth and development and have independence and encouragement in its investigative program. Such a unified objective in teaching will never deprive the inspiring teacher of the opportunity of interesting the student in his own field of work. Third, it may be asked whether a more careful organization of the teaching effort will mean spoon-feeding the student, who presumably enters medical school mature in study habits and capable of independent learning and reflection. Such doubts would also seem unwarranted. The very aims of the program would demand an organization based upon the premise that the student will do as much for himself as he is capable of doing and would foster self-reliance and independence.

I realize that what I have proposed is tentative and untried. One could with reason alter it in many ways. To institute such a program would require careful planning and study. The details would undoubtedly differ from one institution to another. The general principles which underlie the program, and its objectives, would, however, seem sufficiently valid to warrant its careful consideration. I realize too, quite well, that what I have suggested contains little

that is new. From time to time medical educators have expressed in whole or in part similar views. In a few progressive schools initial explorations are being made with similar objectives in mind. I have read many of these suggestions as they were published and have followed these new developments with keen interest. In preparing this address, however, I have refrained from resurveying them in the hope that the spontaneous expression of my own reflections might gain in freshness what it might lose in completeness. I have felt that it was appropriate to bring into the open once again the challenge of a new outlook upon the problem of medical education, and particularly on this one hundredth anniversary of the birth of Halsted. Rather than as a final solution, my proposal has been offered in the hope that it might serve as a catalyst and stimulate others to bring to maturity these simple explorations. If someone could do for general medical education what Halsted did for graduate training in surgery, all mankind would benefit.

RESPIRATORY ACIDOSIS: ITS RELATIONSHIP TO CARDIAC FUNCTION AND OTHER PHYSIOLOGIC MECHANISMS

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DURING the past few years at the University of Minnesota Hospitals we have been actively engaged in the study of respiratory acidosis, particularly as it develops during anesthesia in surgical patients. To date these investigations have dealt principally with the development and application of a portable, rapid gas analyzer and, more recently, with the clarification of those physiologic effects provoked by severe hypercapnia. In this latter regard, one of the most baffling and stimulating of the problems has been the reproducible demonstration of myocardial toxicities, evidenced by ventricular fibrillation, when a high alveolar carbon dioxide tension is rapidly converted to a normal one. A corresponding and equally prompt rise in arterial blood pH takes place, to be sure.

Earlier work by a number of investigators called attention to the high incidence of respiratory acidosis accompanying the usual modern clinical techniques of surgical anesthesiology.[1, 2, 3] Beecher and Murphy reported an average alveolar carbon dioxide level of 13.7 per cent in a series of cases undergoing pneumonectomy.[4] By means of rapid mass spectrometric gas analyses with a portable instrument, we have been able to demonstrate on a surgical service that 35 per cent of the major cases undergoing general anesthesia experience an alveolar carbon dioxide tension of at least twice normal during some 15 minute period of the operation.[5]

If one recalls that most of the general anesthetic agents are respiratory depressants, especially at the level necessary for major surgery, this high incidence rate of hypercapnia is less surprising. An ominous and distressing situation is thus created since few good clinical signs are available to warn of just such a carbon dioxide accumulation. It has been demonstrated that neither a depression of blood oxygen saturation nor cyanosis need appear even with severe degrees of respiratory acidosis.[18] With the respiratory exchange mechanism so impaired in function as to retain CO_2, the acid-base buffering system of the body is seriously impeded. Normally, with the addition of a strong metabolic acid (HA) to the blood stream the following reaction ensues:

$$HA + BHCO_3 \rightarrow H_2CO_3 + BA.$$

When one now relates this reaction to the Henderson-Hasselbalch buffer equation, $pH = pK' + \log\frac{H_2CO_3}{BHCO_3}$, it is apparent that any increase in carbonic

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acid must be associated with a pH depression. With the lungs unable to free the body of carbon dioxide the pH decrease is correctable only slowly and by renal mechanisms. In such a condition, the kidneys preferentially reabsorb fixed base and excrete carbonic acid and chloride, a long-term process which is probably never, or very slowly, carried to completion. Certainly the kidneys would never be able to correct the effect of any major retention of carbon dioxide during the relatively short operative period.

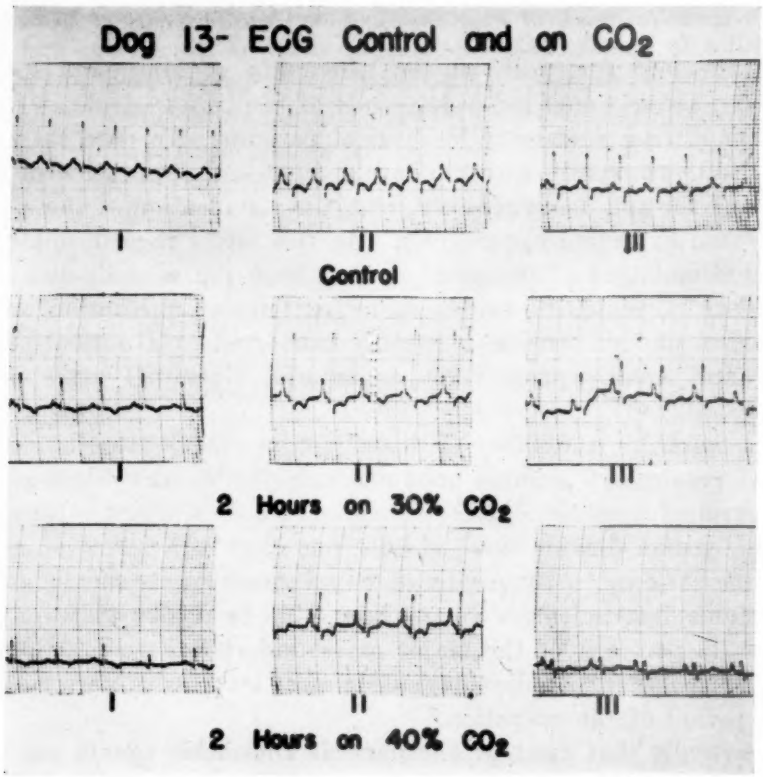

Fig. 1.—A representative illustration of the electrocardiographic patterns obtained with dogs breathing high concentrations of CO_2/O_2. The Roman numerals designate the limb leads.

Taylor and Roos have reported one case in which the arterial pH dropped to 6.86 with this reduction accompanied by a pCO_2 elevation to 170 mm. Hg.[3] Such a pH value is far below the usually accepted minimum for survival, a prevailing belief well summarized by the following quotation from a currently accepted textbook: "The range of hydrogen-ion concentration compatible with life is approximately from one ten millionth to one hundred millionth of a gram per liter. Using the pH notation system the extreme limits of reaction are pH 7.0 and pH 7.8."[6] Most of the fears regarding acidosis can be traced to investigations reported in 1924 by Andrus and Carter, who observed the effects of perfusion of the isolated dog heart with Locke's solution containing an increased hydrogen-ion concentration. They stated that heart block occurred when the pH was carried down to 7.0 or lower.[7] On the other hand, Gertler and Hoff, in 1946, presented the results of similar investigations conducted on experimental

animals rendered acidotic by means of the intravenous infusion of either lactic or hydrochloric acid.[8] They found the lethal level of pH in the dog averaged 6.2. This excellent work denied the existence, in the intact animal, of a phenomenon such as reported by Andrus and Carter in their perfusion studies. Any serious review of pertinent scientific literature thoroughly impresses one with the need for an experimental reassessment of the whole problem of acid-base imbalance during severe degrees of respiratory acidosis. We have therefore undertaken such a study. This broad program, set up for an evaluation of physiologic function and metabolism in animals exposed to an atmosphere of high carbon dioxide and oxygen tensions, permits the study of hypercapnia as an isolated factor without coexisting hypoxia.

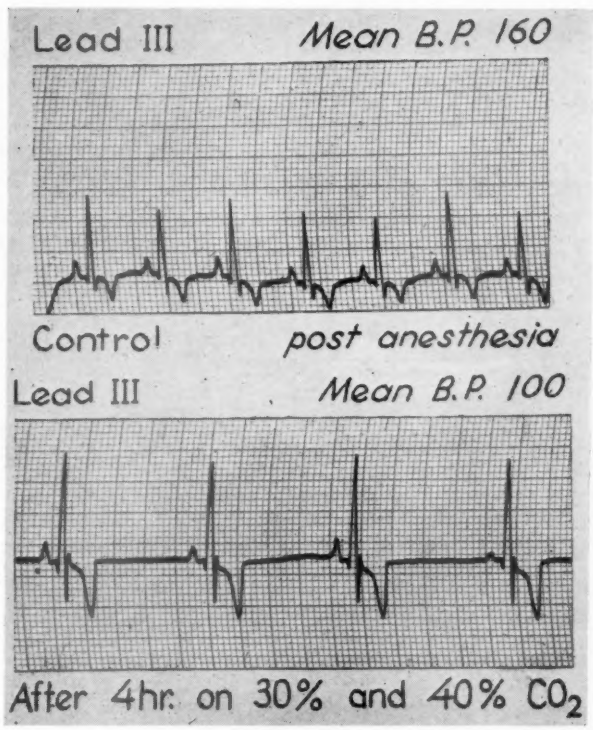

Fig. 2.—Electrocardiograms of dog exposed to hemorrhage plus hypercapnia.

As one phase of this work, respiratory acidosis of sufficient magnitude to depress the arterial blood pH to from 7.0 to 6.7 for periods of 4 to 6 hours, has been induced in more than 50 mongrel dogs. Fig. 1 shows excerpts from sequential electrocardiograms obtained from a typical animal in this series. This tracing, secured while the dog was breathing 40 per cent carbon dioxide, differs from the control only by a slight alteration of the T-wave pattern and some generalized voltage diminution. The only consistent changes we have been able to distinguish in the electrocardiograms made on these acidotic dogs are: (1) A marked bradycardia, and (2) an increased T-wave amplitude. Occasionally in the period directly following the exposure to 30 per cent carbon dioxide the electrocardiogram has shown a few ectopic beats and a slight depression of the

S-T segment associated with temporary blood pressure depression to levels not lower than a mean pressure of 80 mm. Hg. In most instances following this initial drop, the blood pressure returned to a level slightly higher than during the control period and remained there for the remainder of the interval of high percentage carbon dioxide inhalation.

This study was then developed to show the lethal level for acute carbon dioxide exposure. The tests demonstrated the development of respiratory arrest in most instances with the prolonged inhalation of 50 to 60 per cent carbon dioxide in oxygen. The dogs were able to inhale 70 per cent carbon dioxide for 45 minutes before a significant drop in blood pressure occurred and even at these high levels for CO_2 no remarkable electrocardiographic changes appeared.

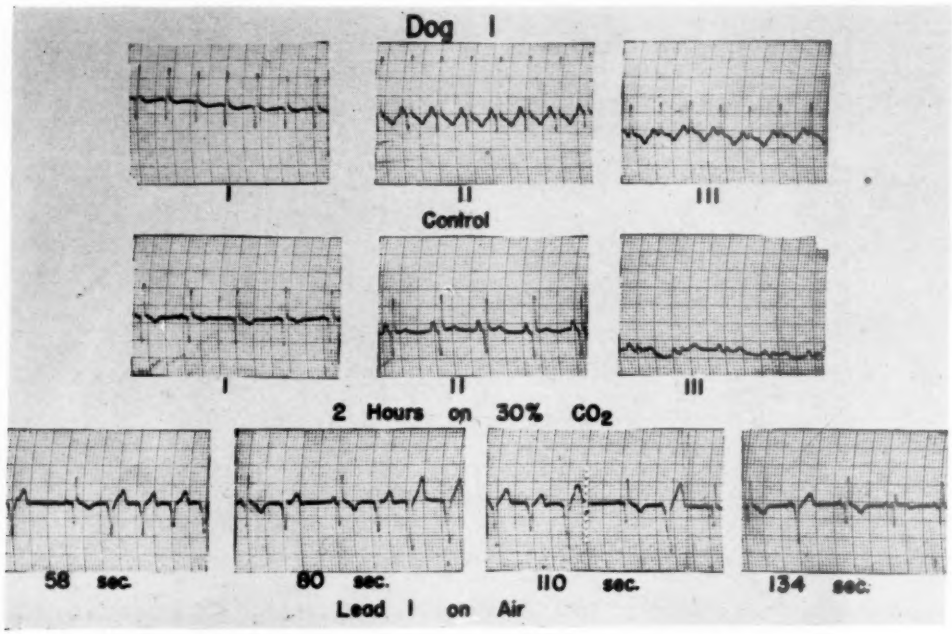

Fig. 3.—Electrocardiograms showing typical results noted when animal switched from 30 per cent CO_2 to air.

If the carbon dioxide concentration was now increased much beyond this point, hypoxia became a contributing factor, yet one dog survived 90 per cent carbon dioxide for 9 minutes with an arterial pH of 6.4.

It is conceded that these experiments represent an assessment of only one variable, namely, hypercapnic acidosis. They do not necessarily portray a true picture, therefore, of the effects of hypercapnia observed clinically, where the addition of coincidental complications (hemorrhage, sepsis, etc.) almost always present in sick patients undergoing major surgery, might be expected to lower the threshold at which various centers or organs might be damaged. The experiments of other observers have shown, too, that vagal stimulation in conjunction with hypercapnia or asphyxia entails additional hazards.[9, 10] We have made occasional observations on dogs malnourished, senile, or coincidentally diseased. With these debilitations, respiratory paralysis may ensue during the inhalation

of 25 to 30 per cent carbon dioxide, and concurrently the blood pressure starts to drop. In Fig. 2 is shown a clear-cut example of sustained electrocardiographic changes accompanying the compounding effects of a severe stress and hypercapnia. This animal had been bled an estimated 300 to 400 c.c. prior to the induction of respiratory acidosis. This tracing evidences changes compatible with a progressive myocardial ischemia, a phenomenon not seen in any of the otherwise unstressed dogs exposed only to prolonged periods of high CO_2 inhalation. The blood pressure tracings for this partially exsanguinated animal show a coincidental depression far below levels usually noted during similar procedures on the normovolemic dogs. This suggests that pH depression is more toxic when accompanied by some real degree of hemorrhage. Clinicians can readily etch with some poignancy the counterpart of this experimental picture from memories of operating room near or real tragedies.

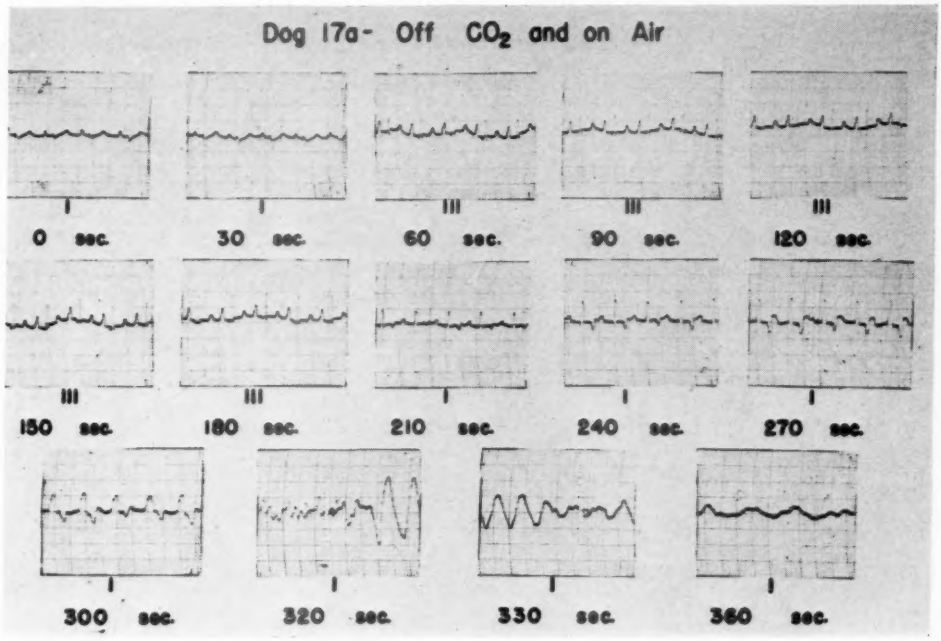

Fig. 4.—Electrocardiograms of one of the initial dogs noted to develop ventricular fibrillation following return to air inhalation after being exposed to 30 per cent CO_2/O_2.

One of the more intriguing, and to date only partially explicable, observations provoked by our carbon dioxide studies, has been the train of events which follows the rapid pH rise toward normal as the hypercapnic animal suddenly breathes room air. A dramatic and demonstrable degree of cardiac malfunction can be noted at this time. Fig. 3 portrays an electrocardiographic pattern with evidence of myocardial irritability appearing after an abrupt switch from the inhalation of 30 per cent carbon dioxide to air. These changes occasionally progress to ventricular fibrillation and cardiac arrest as depicted in Fig. 4. That this animal's electrocardiogram during hypercapnia was not seriously altered is shown in Fig. 5.

Initially the changes of this "posthypercapnic phenomenon" were observed in a group of dogs exposed to the inhalation of serial increments from 15 up to 30 per cent carbon dioxide in oxygen over a period of 4 to 6 hours. The precise minimum degree of respiratory acidosis requisite to provoke a posthypercapnic response is undefined as yet. Too, it might be conjectured that the addition of some abetting disease process might probably cause this acidotic threshold to be altered. We also believe that with this development of a method consistently capable of producing ventricular fibrillation, the technique will ultimately permit an identification of the underlying physiologic mechanisms involved in this phenomenon of ineffectual myocardial twitching. Also, it may well serve as a tool for the study of other basic physiologic cardiac aberrations, in addition to a variety of pharmacologic and other therapeutic considerations.

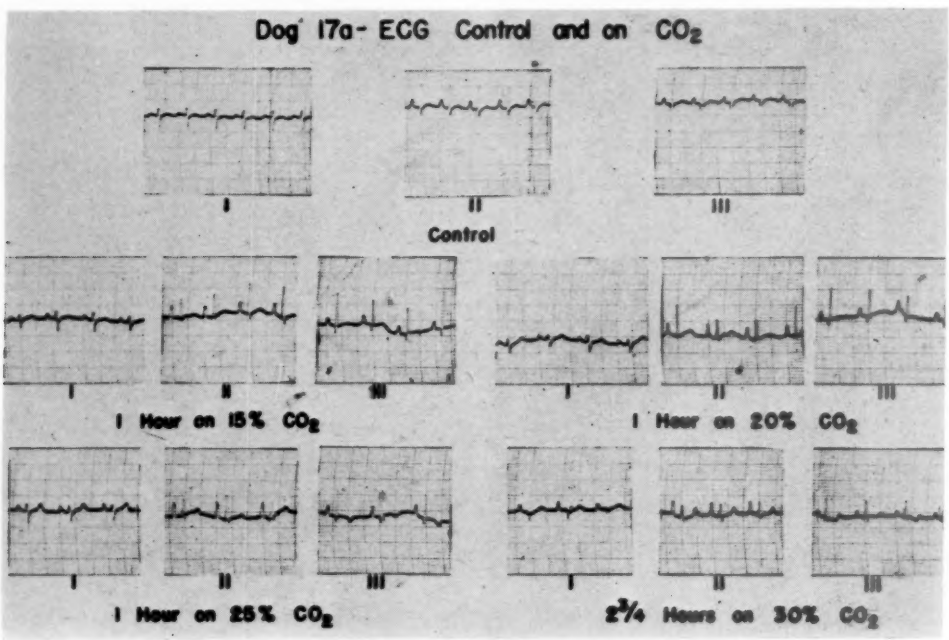

Fig. 5.—Control and hypercapnic records of dog shown in Fig. 4.

This procedure in brief is as follows[5, 11]: Dogs, anesthetized lightly with Pentothal Sodium, in order that tracheotomies and arterial cannulations can be performed, inhale for 2 hours 30 per cent carbon dioxide in oxygen and during the next 2 hour period 40 per cent carbon dioxide in oxygen. At the end of this 4 hour exposure, the carbon dioxide mixture is replaced by air and the animals are artificially ventilated at a rate of 60 respirations per minute with an intermittent positive pressure ventilator. The inspiratory pressure is 15 cm. of water, or less, and the expiratory pressure is atmospheric. Using this technique, the arterial blood pH is rapidly shifted from a level of 6.7 to 7.3 within a 3 minute interval. During the hypercapnia period no Pentothal Sodium is added, since carbon dioxide in the administered concentrations is an adequate anesthetic. In a series of 19 dogs treated by this method, all but 4 died within

10 minutes following the onset of hyperventilation with air. Ventricular fibrillation was the cause of death in the 79 per cent succumbing from this experiment. A typical example of the electrocardiographic response in one of these animals is illustrated in Fig. 6. An analysis of all of the posthypercapnic electrocardiograms showed that a variety of changes might precede the actual onset of ventricular fibrillation. Quite frequently ventricular ectopic beats and evidence of a shifting pacemaker were the first abnormalities discernible. There was occasionally evidence of an S-T segment depression and in some instances a definite auriculoventricular dissociation occurred. The most consistent finding was a prolongation of the QRS component, a finding which is generally assumed to indicate a block or defective interventricular conducting mechanism. Subsequent to this, ventricular tachycardia and ventricular fibrillation appeared. A pronounced elevation or depression of the T-wave amplitude was noted to occur immediately before the ventricular tachycardia in a majority of the cases.

Though 4 animals survived the procedure just described, in only one instance was the electrocardiogram normal throughout the posthypercapnic period of ventilation. The remaining 3 dogs showed quite marked changes even though they recovered.

Table I presents the physicochemical data obtained from a few of the dogs in this series.

TABLE I. PHYSICOCHEMICAL RELATIONSHIPS OF ARTERIAL BLOOD

DOG	PROCEDURE	Hb MM./L.	pH	PLASMA CO_2 CONTENT MM./L.	PLASMA HCO_3 MM./L.	PLASMA H_2CO_3 MM./L.	PLASMA pCO_2 MM. Hg
B	Postanesthesia	7.45	7.43	23.2	22.1	1.1	35.0
	30% CO_2	8.02	6.78	---	---	---	---
	40% CO_2	8.09	6.67	37.9	29.7	8.2	271.0
C	Postanesthesia	4.34	7.36	25.9	24.5	1.4	45.6
	30% CO_2	7.3	6.86	36.8	31.2	5.6	183.8
	40% CO_2	9.75	6.65	46.4	36.0	10.4	343.0
D	Postanesthesia	8.0	7.32	23.0	21.6	1.4	44.2
	30% CO_2	11.1	6.80	---	---	---	---
	40% CO_2	12.0	6.71	38.3	30.5	7.8	259.0
E	Postanesthesia	6.77	7.38	25.4	24.1	1.3	42.8
	30% CO_2	8.5	6.83	38.2	31.1	6.1	202.0
	40% CO_2	8.65	6.69	44.3	35.5	8.8	292.8
H	Postanesthesia	6.21	7.3	24.0	22.8	1.2	38.9
	30% CO_2	8.99	6.76	36.6	29.9	6.7	222.7
	40% CO_2	9.62	6.65	39.7	30.8	8.9	295.5
	Air—7 min.	9.62	7.15	23.3	21.2	2.07	68.9
I	Preanesthesia	9.62	7.38	23.9	22.7	1.2	40.5
	30% CO_2	11.02	6.81	39.3	32.8	6.5	218.0
	40% CO_2	11.49	6.63	47.0	36.2	10.8	362.0
J	Preanesthesia	8.51	7.44	27.8	26.6	1.2	41.2
	30% CO_2	8.05	6.80	41.8	34.7	7.1	218.0
	40% CO_2	8.99	6.69	45.8	36.3	9.5	280.0

Other investigators have noted the canine intolerance to pulmonary insufflation with high positive pressures, either intermittent or continuous.[12, 13] With an awareness of these reports, we adjusted the artificial ventilation so as to keep the maximum level of the positive pressure phase below those pressures reported to be injurious. In order further to reduce this factor the posthyper-

capnic ventilatory procedure was simulated with the anesthetized animal exposed to air before breathing the high carbon dioxide mixtures. Fig. 7 is representative of the electrocardiographic changes observed incident to this procedure. It can be noted that there is only a deviation of the S-T segment from the baseline; this can hardly be a function of hyperventilation, however, since it is also present during the preventilatory control tracing. This dog died of ventricular fibrillation, moreover, during application of the regulation type posthypercapnic procedure described earlier. Dogs similarly hyperventilated while breathing the carbon dioxide mixtures also demonstrated no prognostically grave electrocardiographic abnormalities, nor did they succumb.

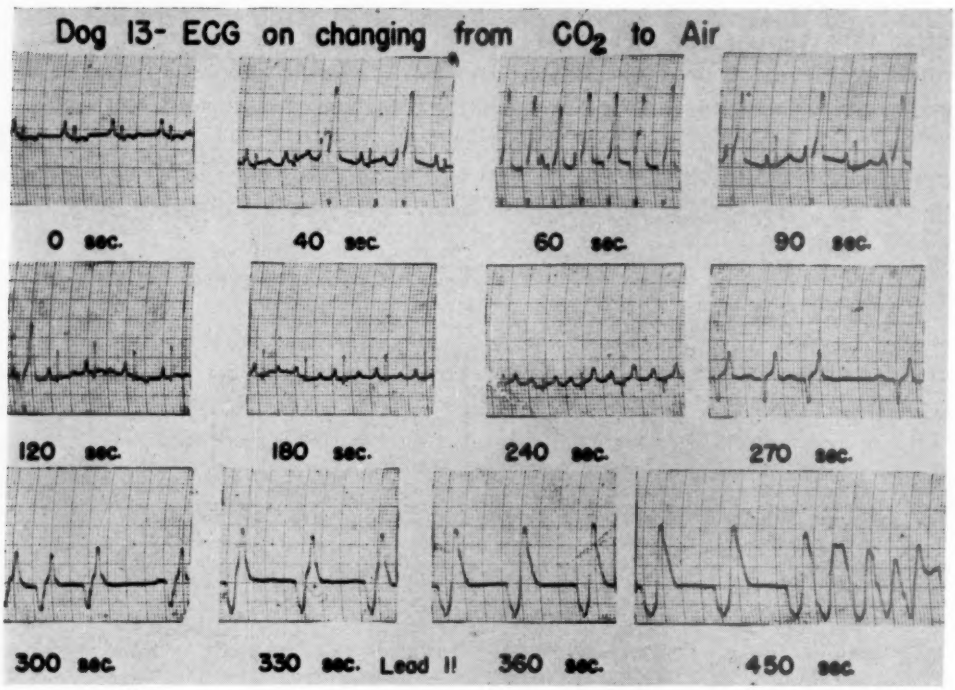

Fig. 6.—Electrocardiograms showing typical results of alterations produced by artificial hyperventilation with air following inhalation of 30 and 40 per cent CO_2/O_2.

During the course of these investigations, hypotension was noted to accompany regularly these posthypercapnic electrocardiographic abnormalities, whereas the hypercapnic mixtures were provocative of an arterial hypertension. The whole reaction seemed roughly analogous to that observed and reported following the removal of a pheochromocytoma. Bodily processes readapt to a chemically induced hypertension so slowly after its abrupt withdrawal that survival is jeopardized.

The exact sequential order of the hypotension and cardiac changes is a matter open to further study. Despite the use of simultaneous electrical recordings of the blood pressure and the electrocardiograms it was impossible to ascertain which of the two changes occurred first due to the insidious nature of the electrocardiographic alterations. In other words, we were unable to determine whether this was primarily a reaction representative of myocardial damage or

whether it might be substantially on the basis of peripheral vascular collapse. True, it did seem difficult to accept the idea that a systolic blood pressure fall to 70 to 80 mm. Hg, the value generally obtained, was injurious enough to produce ventricular fibrillation in such a short time. Nevertheless, to control the situation the hypotensive reaction was corrected by pharmacologic supplementation with a continuous infusion of either 0.002 per cent epinephrine or 0.008 per cent levoarterenol at a sufficient rate to maintain the blood pressure above 100 mm. Hg. This was performed on 7 animals; one died. This high percentage of recoveries was rather unanticipated and further beclouds the problem for, in these 6 surviving dogs, only one had a normal electrocardiogram. Fig. 8 shows the ominous changes noted in a survivor. Others did not manifest changes quite this severe, yet all had marked and prolonged episodes of ventricular tachycardia.

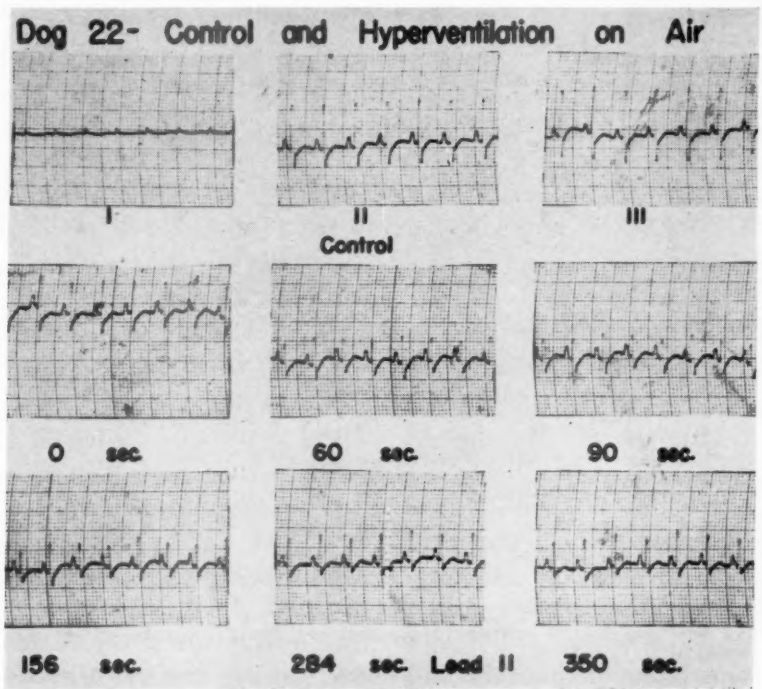

Fig. 7.—Electrocardiograms showing relative absence of changes induced by hyperventilation in air without preceding hypercapnia.

The effect of the drugs as possible provocative mechanisms in this acceleration of ventricular rate is acknowledged, still, the ventricular tachycardia would upon occasion revert to a normal pace despite maintenance of an infusion of the vasoconstrictor agents. Quite conceivably, also, the lifesaving effect of these pharmacologic materials might be related to yet another action than that of vasoconstriction.* Other methods have been tested unsuccessfully in attempting to avert the electrocardiographic changes and/or the animals' death. The only technique uniformly lifesaving and unaccompanied by electrocardiographic

*Of 3 dogs first quinidinized and then submitted to inhalation of high concentration of carbon dioxide for several hours, followed by its abrupt withdrawal, 2 survived. The series is being expanded.

changes is that of bringing about a gradual reduction of the blood carbon dioxide tension. This has been safely accomplished by a graduated type of hypoventilation or by decreasing slowly the concentration of inhaled carbon dioxide, as during a period of 15 to 30 minutes.

We are left with the presumptively logical conclusion that a hypotension does serve to potentiate a myocardial damage induced by the sudden pH rise or decrease in alveolar carbon dioxide tension occurring during the "posthypercapnic phenomenon."

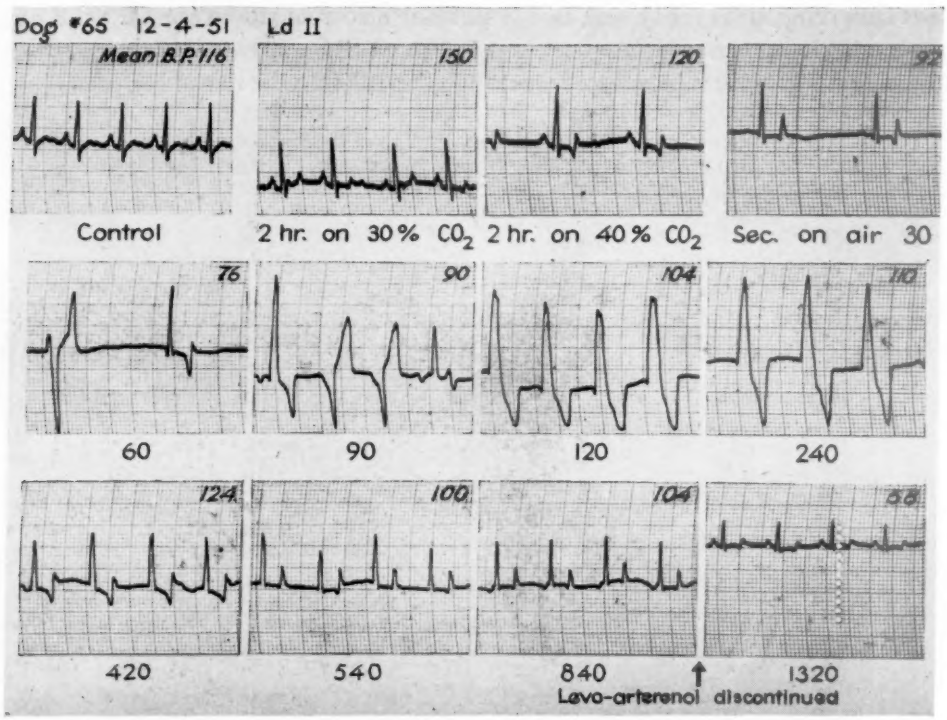

Fig. 8.—Electrocardiograms of an animal supplemented by levoarterenol to maintain blood pressure during posthypercapnic period. Note that the blood pressure did drop a little during the first 90 seconds.

The question of whether anoxemia plays any part in this "posthypercapnic phenomenon" was considered, for some of the animals had tracings with an S-T segment depression, suggestive of myocardial anoxia. Chemical analyses of the arterial blood during this period revealed oxygen saturations ranging around 90 per cent or greater. The feasibility of anoxic anoxia was additionally controlled by hyperventilating 2 dogs, after the usual period of preparation with CO_2, with oxygen instead of with air. Each died promptly. The evidence against anoxemic deaths seems irrefutable. To test a hypothesis that myocardial ischemia from coronary constriction provoked the lethal effects noted, amyl nitrite, a known coronary vasodilator was tried without beneficial effects. Pronestyl, a procaine amide, was given without apparent therapeutic effect either prophylactically or for controlling arrhythmias already present. In 2

dogs, the intravenous and intracardiac injections of 10 c.c. of 10 per cent calcium gluconate either before or during the posthypercapnic phase were without life-saving consequences. Intracardiac Coramine injections were also ineffective.

At the present time we are continuing the investigation of the specific mechanisms provoking the cardiac abnormalities described above. Our attention has been attracted to the not necessarily fortuitous similarity of the electrocardiographic patterns represented in Figs. 4 and 6 with those characterizing certain cases of hyperpotassemia.[14] It is possible that the myocardial changes observed in our experiments might be the resultant of sudden alterations in the potassium concentrations in either the serum or cells. Studies are currently under way in our laboratory to evaluate this possibility. In addition, the contribution of hypotension is to be examined more thoroughly.

DISCUSSION

A critical phase occurring right after the abrupt switch-over to air in a patient with induced severe respiratory acidosis has been called the "posthypercapnic phenomenon." The clinical significance of this phase has been given impetus by Dripps' identification of an interlude he has named as "cyclopropane shock," transpiring as a possible sequel of the carbon dioxide blow-off just after a period of hypercapnia.[15] His suggestion has recently been definitely affirmed and elaborated upon by us in clinical tests utilizing the mass spectrometer.[16] It was reasoned that a potential and causal relationship of the "posthypercapnic phenomenon" to certain heretofore unexplained cardiac arrests existed and merited more detailed study. In the absence of direct confirmatory evidence for such a conjectured correlation, we felt that a review of the recent cases of cardiac disasters might be informative. A very brief résumé of the most interesting of these findings will be presented.

Among all surgical deaths during the 28 month period from July, 1948, through October, 1950, at the University of Minnesota Hospitals were 14 fatalities associated with cardiac arrest from all causes and transpiring during or immediately following surgery. During this same interval approximately 12,000 cases were anesthetized, an incidence of roughly 0.11 per cent. In all but one of the fatal cases, there was primary, bona fide, and sometimes advanced cardiac disease, diagnosed either by preoperative studies or post-mortem examination. The likelihood that pre-existing cardiopathy potentiates the lethal effects of hypercapnia is almost inescapably self-evident. In 6 of the cases death occurred shortly after tracheal intubation or extubation. These findings are very similar to those reported by Shumacker and Hampton, who noted five cardiac surgical deaths shortly after removal of the endotracheal tube.[17]

The re-examination of our cases revealed one instance in which there was definite evidence for the implication of carbon dioxide in the unfortunate end result.

G. K. (No. 802886), a 2½-year-old boy, was taken to surgery for skin grafting. He had been burned a number of weeks previously and had been anesthetized on 2 previous occasions without apparent ill effects. Cyclopropane was used on this occasion. The anesthetist reported respiratory difficulty throughout the procedure. Twenty minutes before the

conclusion of the case, he attempted to stimulate the depth of respiration by adding carbon dioxide (concentration unknown) to inhaled gaseous mixture. The added carbon dioxide was continued throughout the remainder of the case. The total duration of anesthesia was 2 hours. The patient was returned to the postoperative recovery room where his blood pressure was recorded at 112/50 and respirations were noted as jerky. Forty-five minutes later cardiac arrest occurred. Cardiac massage was effective in restarting the heart but a short time later the arrest recurred and this time manual manipulation failed.

In view of the insidious ease with which carbon dioxide accumulates during cyclopropane anesthesia, together with a factual recording of its being added to the mixture of gases being inhaled, this tragic sequence carries a disturbingly familiar resemblance to descriptions noted under "posthypercapnic phenomenon."

CONCLUSION

We submit, as a result of these investigations, that a patient, after a prolonged and severe siege of respiratory acidosis, hovers on the brink of disaster if suddenly ventilated with a mixture low in carbon dioxide composition. This clearly outlines the necessity for adequate pulmonary ventilation in all patients subjected to general anesthesia. Where no special devices are available for measurement of alveolar carbon dioxide or tidal exchange, the sustained and competent supplementation of respiration throughout the period of anesthetization is mandatory and may be lifesaving.

SUMMARY

A brief review of the physiologic mechanisms involved, plus the incidence rate of respiratory acidosis in the clinical practice of anesthesia has been presented.

An observation which we have entitled the "posthypercapnic phenomenon" is described. This consists of cardiac arrhythmias and/or arrest following the sudden reversal of a hypercapnic state toward normal by means of rapid hyperventilation. Methods were described for diminishing the lethality of this reaction. A possible relationship between this experimental observation and certain clinically unexplained cardiac arrests occurring during surgery or immediately thereafter has been offered.

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DISCUSSION

DR. JOHN H. GIBBON, JR.—I think this is a beautiful piece of work. It offers an explanation of the drop in blood pressure which sometimes occurs at the conclusion of an intrathoracic operation. Some surgeons have observed such declines in blood pressure at the conclusion of an operation and have attributed them to the change in position which occurred when the patient was moved from the operating room table to a stretcher. I think this is an excellent demonstration of the fact that such drops in blood pressure can probably be accounted for by the rapid elimination of CO_2, with the return to a normal pH, in an inadequately ventilated patient at the end of a long operative procedure. I hope that we will have, sometime in the near future, a simple and easy method like a mass spectrophotometer to do the job of recording continuously during the course of an operation the CO_2 tension of the arterial blood. Perhaps the infrared method of analyzing the expired air may prove simpler than using a mass spectrophotometer.

SIGNIFICANCE OF PULMONARY HYPERTENSION IN CONSTRICTIVE PERICARDITIS

A Pre- and Postoperative Study

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(From the Surgical Services and Cardiac Laboratory of the Massachusetts General Hospital)

STUDY of the circulation by means of the cardiac catheter has afforded the opportunity to test, in the intact patient, established concepts of cardiac disease. Now that direct observations of pressure and volume flow are possible in hitherto inaccessible areas of the circulatory system, it is not surprising that attention has been redirected to the hemodynamic changes that occur in constrictive pericarditis. Accumulating evidence supports the view that, in general, both the right and the left side of the heart are similarly affected in this disease and that inflow stasis is the result of encasement and interference with ventricular function, rather than encroachment upon the right atrium and orifices of the great veins. It is the purpose of this report to present direct evidence in support of these concepts and to emphasize the need to liberate *both* ventricles in order to relieve the *pulmonary* hypertension which regularly accompanies elevated peripheral venous pressure in chronic constrictive pericarditis.

In 1951, Burwell and his associates[1] reported cardiac catheterization studies of four patients with constrictive pericarditis and concluded that individuals who have an elevated peripheral venous pressure associated with pericardial disease can be assumed to have a degree of congestion in the lungs similar to that which exists in the periphery. Their evidence clearly suggested that the function of both the right and left ventricles was seriously impaired in these patients. They found virtually identical pressures in the superior and inferior venae cavae and the right atrium, and these closely approximated the right ventricular end-diastolic pressure. For this reason they concluded that there was no pressing need to decorticate the right atrium and great veins. This conclusion is distinctly at variance with the published opinion of Holman[4] who has emphasized the need to liberate these structures and has therefore recommended median sternotomy as the preferred method of surgical approach.

Isaacs[5] has recently reported cardiac catheterization studies of dogs in which he has produced, and then corrected, chronic constrictive pericarditis involving the whole heart or any combination of its chambers. His findings confirm the importance of functional impairment of both ventricles as a result of interference with their diastolic filling. His experimental data correlate remarkably well with the clinical and laboratory data obtained in a study of the patients who are the subject of this report.

This study was supported by a research grant from the National Heart Institute of the United States Public Health Service.

Read at the meeting of the Society of University Surgeons, Baltimore, Md., Feb. 7-9, 1952.

In 1948 our attention was called[8] to the presence of pulmonary hypertension in patients with constrictive pericarditis who required reoperation directed toward the left side of the heart in order to obtain satisfactory relief of symptoms. In the past four years we have had the opportunity to study by cardiac catheterization ten patients with chronic constrictive pericarditis. In five of these we have been able to repeat the study after a postoperative interval of five to forty-three months. This latter group of five are here reported in detail.

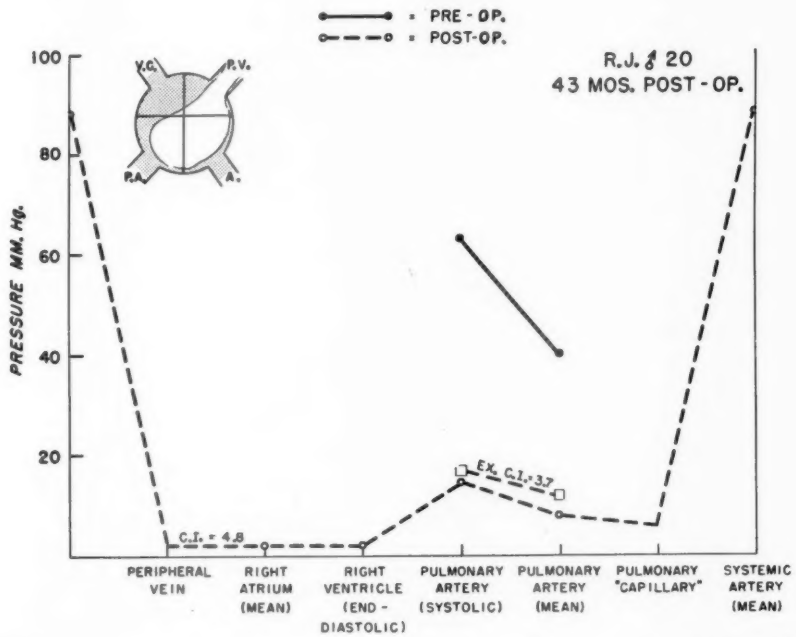

Fig. 1 (Case 1).—Record of pressures at various stations in the circulatory system showing return to normal levels forty-three months after pericardiectomy. Diagram in the left upper corner represents the extent of pericardial resection (unshaded area) with respect to the four chambers of the heart. V.C.—vena cava, P.V.—pulmonary vein, A.—aorta, P.A.—pulmonary artery, C.I.—cardiac index (cardiac output in liters per minute per square meter of body surface area), Ex.—exercise. The method of presentation is similar to that of Burwell.[1]

Cardiac catheterization was carried out under fluoroscopic control. A Sanborn electromanometer was used to measure and record pressures. Pulmonary capillary pressures were obtained by obturating a terminal branch of the pulmonary artery.[2] The oxygen content of blood samples was determined by the Van Slyke method. Oxygen consumption was measured by collection of expired air and Haldane analysis of its oxygen and carbon dioxide content. A standard exercise was used. In this the patient's legs were allowed to bend at the knee over the end of the fluoroscopic table. The patient was then instructed to kick each leg alternately to the horizontal to a metronome count of 80 per minute. Simultaneous pulmonary and radial artery blood samples and expired air were obtained during the last minute of a two-minute period of exercise. Pressures were recorded at the close of the two-minute period.

CASE 1.—The first patient, R. J. (MGH 598813), was 20 years old at the time of the preoperative study in 1947. During the ten months prior to hospitalization, he had been severely handicapped by abdominal swelling and dyspnea on exertion. There had been many

syncopal attacks. He presented the classic appearance of chronic constrictive pericarditis with emaciation, a grossly protuberant abdomen, and distended, pulsating neck veins. The peripheral venous pressure was 270 mm. saline solution. The systemic blood pressure was 110/70. A paradoxical pulse was noted. The heart sounds were of good quality although the rhythm was grossly irregular. The pulmonic second sound was increased. Cardiac catheterization was carried out in December, 1947. This was the first patient catheterized in our laboratory and our observations were limited to the resting pulmonary pressure. The data are presented in Fig. 1. Preoperatively the pulmonary artery pressure was 63/32 with a calculated mean of 42 mm. Hg. (Normal 25/10 with a mean of 15 mm. Hg.)

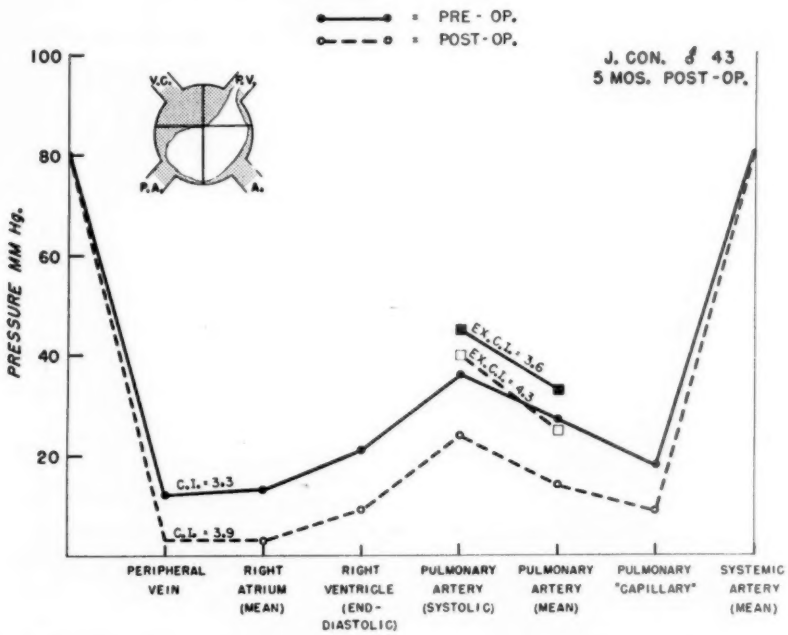

Fig. 2 (Case 2).—Pre- and postoperative record showing satisfactory return toward normal levels five months following pericardiectomy. There is still a definite rise of pulmonary artery pressure in response to exercise postoperatively, and some elevation of the right ventricular end-diastolic pressure.

The patient was operated upon Dec. 5, 1947. A left anterolateral approach was used with resection of the fifth costal cartilage and extension of the incision laterally in the fifth intercostal space. A large plaque of calcification was found over the left auricle, left pulmonary veins, and upper portion of the left ventricle. The pericardium over the right ventricle was thickened but contained little calcification. Pericardiectomy was carried out so as to free completely the left ventricle and the lower portion of the left auricle as far posteriorly as the entrance of the left pulmonary veins. The anterior surface of the right ventricle was also liberated, but no effort was made to free the right auricle or the venae cavae. The patient's postoperative response was excellent. Despite persistent auricular fibrillation and slight cardiac enlargement, he showed no evidence of congestion and was normally active, working as an accountant, three months postoperatively.

Postoperative catheterization was carried out 43 months postoperatively. The data are presented in Fig. 1 and fall well within the limits of normal. Right atrial and right ventricular end-diastolic pressures were low, approaching zero; the pulmonary artery pressure was well within normal limits and failed to rise appreciably on exercise. At this time the right ventricular pressure curve was normal.

The patient was receiving digitalis at the time of the postoperative, but not the preoperative study.

CASE 2.—The second patient, J. Con., (MGH 699299), was a 43-year-old refrigerator worker who, four months before admission on April 24, 1950, had been hospitalized elsewhere because of ascites, peripheral edema, hydrothorax, and cardiac enlargement. At that time symptoms were partially relieved by rest and mercurial diuretics. Following his return to work, ankle edema, dyspnea on effort, and mild orthopnea reappeared. He was then referred to the Massachusetts General Hospital with a diagnosis of congestive heart failure. On examination the heart appeared to be slightly enlarged, a third heart sound was well heard,

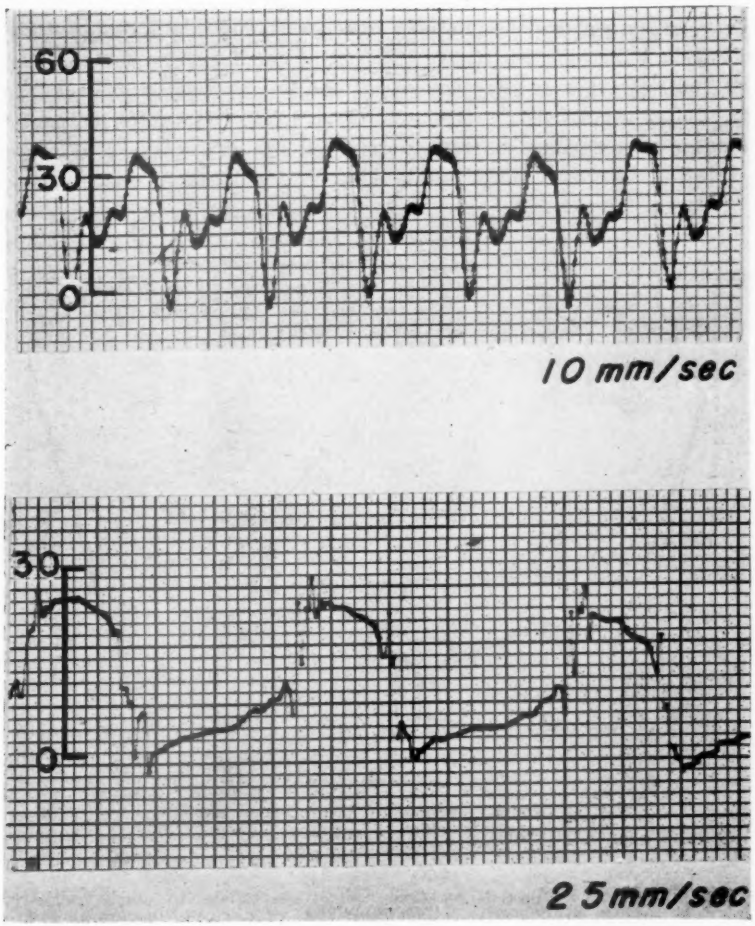

Fig. 3 (Case 2).—Right ventricular pressure curves before and after pericardial resection for constrictive pericarditis. Pressures measured in mm. Hg. Preoperative tracing (above) shows early diastolic fall and prompt rise to end-diastolic pressure. The second diastolic dip is not in keeping with the expected plateau pattern, but probably represents artefact. Postoperative tracing (below) shows gradual rise of diastolic pressure to a somewhat elevated end-diastolic level.

and the pulmonic second sound was accentuated. The blood pressure was 128/84. No paradoxical pulse could be demonstrated. The neck veins were prominent and pulsating. The liver was readily palpable in spite of ascites, and marked ankle edema was present. Fluoroscopic examination of the heart showed no abnormality of the cardiac pulsations and no pericardial calcification. An electrocardiogram was grossly abnormal and consistent with a diagnosis of constrictive pericarditis. In order to establish the diagnosis, a limited pericardial exploration was carried out under local anesthesia on May 22, 1950. At that time a dense, adherent pericardium was demonstrated. Cardiac catheterization was performed on June 2, 1950 (Fig. 2).

In the preoperative study, a marked elevation of the peripheral venous pressure in both superior and inferior venae cavae was apparent. Significantly this was identical with the pressure in the right atrium. The right ventricular end-diastolic pressure was high. The right ventricular pressure tracing (Fig. 3) showed the characteristic early diastolic dip with rapid rise of the diastolic pressure and plateau described by Hansen.[3] The pulmonary artery pressure was high and increased significantly on exercise, although the cardiac index rose but slightly under these conditions. The pulmonary capillary pressure was elevated, indicating elevation of the pulmonary venous pressure similar to that in the peripheral veins.

On June 16, 1950, pericardiectomy was done. An anterolateral approach through the fifth intercostal space with resection of the fifth costal cartilage was chosen. Total decortication of the left ventricle back to the entrance of the left inferior pulmonary vein and superiorly along the auriculoventricular groove was carried out. The anterior, and two-thirds of the inferior, surface of the right ventricle were freed but the entrance of the superior vena cava and the inferior vena cava could not be clearly visualized.

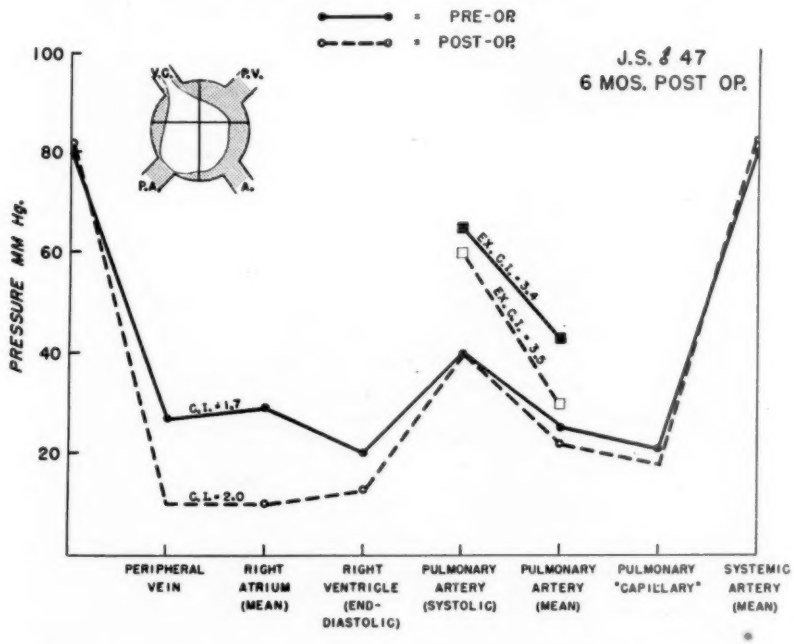

Fig. 4 (Case 3).—Pre- and postoperative record of patient in whom pericardiectomy was carried out through median sternotomy. The elevation of peripheral venous pressure has been improved, but there is little change in the degree of pulmonary hypertension. Note great rise of pulmonary artery pressure in response to exercise.

The postoperative course was entirely satisfactory. The patient returned to good health within three months and was economically rehabilitated within five months. Catheterization studies four months postoperatively demonstrated a return toward the normal (Fig. 2). At this time there was no evidence of increased peripheral venous pressure, the right atrial pressure was within normal limits, the pulmonary artery and pulmonary capillary pressures were normal at rest in spite of an increase in cardiac index over the preoperative value. The pulmonary artery pressure, however, did rise abnormally with exercise coincident with a moderate rise in cardiac index over the resting level. The right ventricular pressure curve no longer showed a diastolic plateau, although there was a gradual rise of right ventricular diastolic pressure to an end point of 9 mm. Hg (Fig. 3).

The patient was receiving digitalis at the time of both the preoperative and postoperative studies.

CASE 3.—The third patient, J. S. (MGH 724396), was a 47-year-old commercial traveler who was admitted to the Baker Memorial Hospital on Dec. 28, 1950. Thirteen months before admission the patient had consulted his family physician because of exertional dyspnea. A tentative diagnosis of coronary heart disease with congestive failure was made. In the course of the next few months the patient became progressively incapacitated by ankle edema and ascites which required several abdominal taps to relieve dyspnea. The symptoms were not relieved by digitalis, dietary restrictions, rest, and mercurial diuretics. By the time of admission to this hospital, the patient presented the classic picture of constrictive pericarditis, including a distinct third heart sound. Extensive calcification of the pericardial sac was noted on x-ray examination. Cardiac catheterization was carried out on Jan. 5, 1951.

The preoperative catheterization data of this patient are presented graphically in Fig. 4. There is uniform elevation of the superior vena caval, right atrial, and right ventricular end-diastolic pressures. The pulmonary artery pressure is significantly elevated at rest and rises to impressive levels on exercise coincident with a twofold increase in cardiac index. The pulmonary capillary pressure is also significantly elevated to a mean of 25 mm. Hg. A marked early diastolic dip and late plateau was noted in the right ventricular pressure curve.

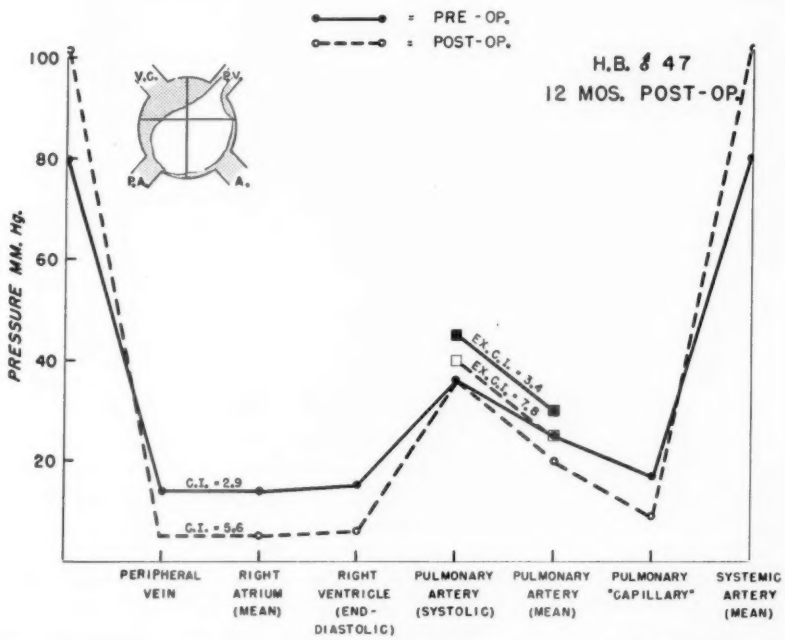

Fig. 5 (Case 4).—Pre- and postoperative record of patient in whom there was return to normal pressures on the right side of the circulation postoperatively, but persistence of almost the same degree of pulmonary hypertension. Cardiac index was greatly increased postoperatively. Peripheral systolic hypertension had also developed.

The patient was operated upon Jan. 11, 1951. A median sternotomy, extending from xiphoid to sternal notch, was used. The operative note describes a large, irregular, calcified plaque extending along the inferior, diaphragmatic surface of the heart. The calcified process was not so dense over the apex of the heart but did encompass the auriculoventricular groove on the left. Dissection was carried to the left "as far as and somewhat behind the phrenic nerve and to the right as far as the vena cava." The patient's postoperative course was satisfactory.

The patient returned six months postoperatively for evaluation. At that time he was active and had no complaints. However, there was moderate cardiac enlargement and distention of neck veins. Ankle edema had not completely disappeared. Cardiac catheterization

showed considerable reduction of the right atrial and right ventricular end-diastolic pressures (Fig. 4). However, pulmonary hypertension was present at rest and on exercise, with only slight improvement over the preoperative levels. Satisfactory pulmonary capillary pressures were not obtained. The postoperative right ventricular pressure curve showed the persistence of some plateau effect, though less marked than preoperatively.

The postoperative data on this patient are consistent with a less complete liberation of the left ventricle than the right. This is implied in the operative note. One cannot, of course, exclude some degree of myocardial failure. This patient was receiving digitalis at the time of both the preoperative and postoperative studies.

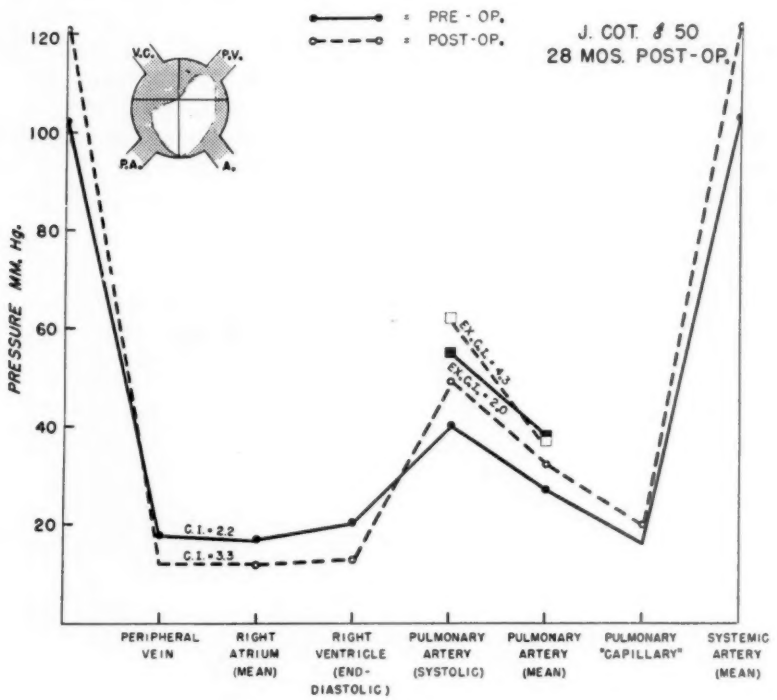

Fig. 6 (Case 5).—Pre- and postoperative record of pressures in a patient in whom left heart failure was present postoperatively. There is some improvement in the peripheral venous pressure, but increase in the pulmonary hypertension following operation.

CASE 4.—The fourth patient, H. B. (MGH 703234), was a 47-year-old steamfitter who had noted the gradual increase of abdominal girth for five years. This had been associated with incapacitating dyspnea during the past six months. Ankle edema had been present for one year. The physical examination was entirely consistent with a diagnosis of constrictive pericarditis. There were distended, pulsating neck veins and marked paradoxical pulse. The blood pressure was 120/80. The pulmonic second sound was accentuated. A third heart sound was present. Roentgenograms of the chest showed no pericardial calcification and it is also of interest that normal pulsations were noted fluoroscopically. Preoperative cardiac catheterization was carried out on June 9, 1950. The findings are presented in Fig. 5. It is to be noted that peripheral venous, right atrial, and right ventricular end-diastolic pressures are all elevated to 15 mm. Hg. Moderate pulmonary hypertension, increasing with exercise, is evident. The cardiac index is not fixed, but rises significantly with exercise. Pulmonary capillary pressure is elevated. An early diastolic dip and late plateau were present in the right ventricular pressure tracing.

The patient was operated upon July 20, 1950, through a left anterolateral approach with resection of the anterior end of the fifth rib and costal cartilage. The entire pericardium was found to be thickened especially over the left ventricle and atrioventricular

groove. The constricting scar over almost the entire left ventricle, the anterior surface of the right ventricle, the left auricular appendage, and the entrance of the left inferior pulmonary vein into the atrium was resected. The patient had an uneventful postoperative course with prompt subsidence of the clinical evidence of elevated peripheral venous pressure. He returned to light work within four months and within eight months was again fully active as a steamfitter. There was no further ascites, ankle edema, or exertional dyspnea.

The patient returned for study approximately one year postoperatively. At that time (Fig. 5) there was no evidence of increased peripheral venous pressure. The right atrial and right ventricular diastolic pressures were within normal limits. A slight degree of pulmonary hypertension at rest and with exercise was still present. The pulmonary capillary pressure was at the upper limits of normal. Postoperatively there was peripheral systolic hypertension coincident with a rise in cardiac index and a calculated increase in stroke output.

This patient received no digitalis before the preoperative or postoperative studies.

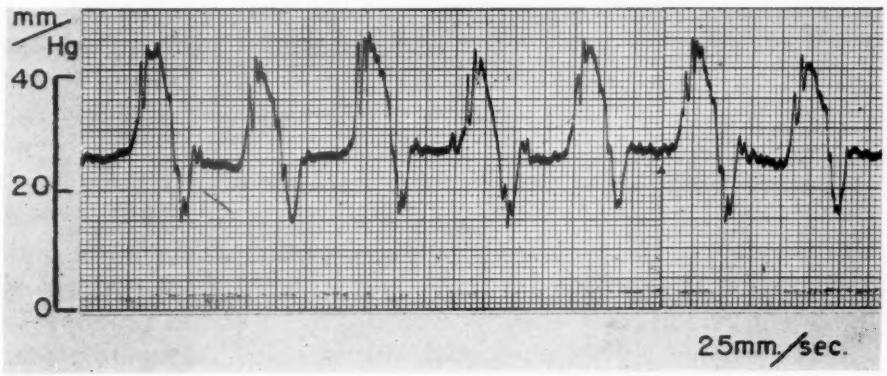

Fig. 7 (Case 5).—Right ventricular pressure curve in constrictive pericarditis demonstrating clearly an early diastolic fall with prompt rise to an elevated end-diastolic level which is then maintained as a plateau through the balance of diastole.

CASE 5.—The fifth patient, J. Cot. (MGH 649876), was 50 years old and by far the most severely ill patient of those we have studied. He was admitted to the hospital on Jan. 25, 1949, with a long and complicated history of frequently recurrent episodes of generalized edema, ascites, and dyspnea on exertion over a period of twenty years. For three years prior to admission he had led a bed-and-chair existence. The heart was normal in size with regular rhythm. The pulmonic second sound was markedly accentuated. The neck veins were distended and pulsating. The liver was grossly enlarged and ascites and ankle edema were present. The blood pressure was 125/90. The patient had received digitalis.

Cardiac catheterization was carried out on Feb. 4, 1949 (Fig. 6). The mean pressure in the superior vena cava and right atrium and the right ventricular end-diastolic pressure were elevated to 18-20 mm. Hg. There was moderate pulmonary hypertension rising on mild exercise to 55/35 with a mean of 38 mm. Hg. The pulmonary capillary pressure was not measured. The right ventricular pressure curve showed a pronounced early dip and late diastolic plateau pattern (Fig. 7). The cardiac index did not increase with exercise.

Pericardiectomy was performed on Feb. 18, 1949, through an anterior incision with resection of the fifth costal cartilage and anterior end of the fifth rib. It was estimated that two-thirds of the left ventricle and one-half of the right ventricle were liberated. The left auricle was exposed but not completely freed, and the diaphragmatic aspect of the pericardium was not removed. Considerable invasion of the left ventricular wall by calcium was noted.

The patient's postoperative improvement was slow and complicated by a cerebrovascular accident on the third postoperative day. At the end of six weeks he was discharged for

TABLE I. CHRONIC CONSTRICTIVE PERICARDITIS; PRE- AND POSTOPERATIVE CARDIAC CATHETERIZATION DATA

	CASE 1 R. J. ♂ 20		CASE 2 J. CON. ♂ 43		CASE 3 J. S. ♂ 47		CASE 4 H. B. ♂ 47		CASE 5 J. COT. ♂ 50	
	PREOP.	43 MO. POSTOP.	PREOP.	5 MO. POSTOP.	PREOP.	6 MO. POSTOP.	PREOP.	12 MO. POSTOP.*	PREOP.	28 MO. POSTOP.†
Pressure (mm. Hg)										
Inf. vena cava	—	—	12	—	—	—	14	—	—	—
Sup. vena cava	—	—	12	—	27	—	14	—	18	—
Rt. atrium: mean	—	2	13	3	29	10	14	5	17	12
Rt. vent. end-diast.	—	2	21	9	20	13	15	6	20	13
Pul. art—rest	63/32	16/4	36/15	24/10	40/20	40/16	36/20	36/10	40/20	49/22
Pul. art—exercise	—	18/6	45/24	40/15	65/34	60/20	45/26	40/10	55/35	62/27
Pul. art: mean-rest	40	8	27	14	25	22	25	20	27	32
Pul. art: mean-exercise	—	12	33	25	43	30	30	25	38	37
Pul. capillary	—	—	18	9	21	—	17	9	—	20
Syst. art: mean-rest	—	88	80	80	80	82	80	102	102	121
Syst. art: mean-exercise	—	85	75	95	87	100	96	114	—	116
Cardiac index-rest	—	4.8	3.3	3.9	1.7	2.0	2.9	5.6	2.2	3.3
Cardiac index-exercise	—	3.7	3.6	4.3	3.4	3.5	3.4	7.8	2.0	4.3
Stroke output-rest	—	120	104	101	62	80	59	114	43	85
Stroke output-exercise	—	82	100	107	92	125	63	143	38	98

*Definite systolic hypertension postoperatively. 160/88 at rest, 180/78 on exercise; 120/80 preoperatively.

†Auricular fibrillation postoperatively with left ventricular failure. Systemic pressure has risen from 125/90 to 150/71 at rest.

convalescent care. He was not rehabilitated, although gradually over the next ten months there was significant improvement over his preoperative status. Auricular fibrillation and gradual cardiac enlargement developed.

The patient returned for re-evaluation and repeat cardiac catheterization twenty-eight months after operation (Fig. 6). At this time, systolic hypertension of 185/87 at rest was present. Peripheral venous pressure, right atrial and right ventricular end-diastolic pressures were somewhat lower than preoperative levels. The pulmonary hypertension, however, had increased. In view of the cardiac enlargement left ventricular failure was suspected, although persistent or recurrent constriction of the left heart could not be excluded. The patient was still receiving digitalis. He continued his semi-invalid life and has recently died at home. A limited autopsy showed that there remained considerable constricting scar over the postero-lateral half of the left ventricle, preventing adequate liberation of that chamber.

DISCUSSION

Certain common factors are apparent in the preoperative studies of the five patients here presented. In all, significant pulmonary hypertension was found. This was consistently associated with an elevated pulmonary capillary pressure which has been shown to approximate pulmonary venous pressure. An elevated pulmonary venous pressure reflects some obstruction to blood flow through the left side of the heart. Since there is no evidence of valvular disease in these patients, it is reasonable to attribute this obstruction to interference with diastolic filling of the left ventricle due to the constricting pericardium with or without some degree of myocardial failure. Where some degree of pulmonary hypertension persists after operation, it is impossible to differentiate how much may be attributed to residual scar and how much to myocardial failure. There seems to be little reason to suspect constriction of the pulmonary veins as the cause of the elevated pulmonary venous pressure. It is interesting to note that in a study of 53 patients, Paul, Castleman, and White found that shortness of breath on effort was the most frequent initial symptom of constrictive pericarditis.[7]

A second common factor is the marked elevation of right ventricular end-diastolic, right atrial, and peripheral venous pressures to a virtually uniform level. This finding corroborates the observations of Burwell and Isaacs and immediately rules out constriction of the great veins as a significant factor. We were not able to demonstrate a significant difference in pressure between the superior and inferior vena cava.

Presumptive evidence for interference with diastolic filling is found in a study of the preoperative right ventricular pressure curves. In all there is an early diastolic fall, followed by a prompt sharp rise to an elevated end-diastolic level which is then maintained as a plateau through the balance of diastole. The characteristic nature of this curve has been discussed at length by Hansen et al.[3] It is of interest that the plateau had disappeared or was greatly reduced in the postoperative study of all our patients. As pointed out by McKusick,[6] the third heart sound which is frequently heard in patients with constrictive pericarditis is probably the result of abrupt filling of the ventricle early in diastole.

Classically it has been emphasized that patients with chronic constrictive pericarditis have a low fixed cardiac index. However, two of the four in whom

the cardiac index was calculated preoperatively proved to be exceptions to this rule in that they showed a significant increase of cardiac index in response to mild exercise without a corresponding rise of pulse rate (Cases 3 and 4). In two patients (Cases 4 and 5) definite peripheral systolic hypertension was noted postoperatively. In both, this was associated with a significant rise in resting cardiac index and stroke output. It may, therefore, reflect the response of a rigid vascular tree to increased blood flow.

CONCLUSIONS

1. In all of the cases studied, pulmonary hypertension was a constant feature of chronic constrictive pericarditis. This is evidence for involvement of the left side of the heart by the constrictive process. By adequate pericardiolysis of the left ventricle, pulmonary hypertension may be completely relieved. Pulmonary hypertension that persists after pericardial resection may be attributed either to residual constricting scar or to some degree of left ventricular failure.

2. Elevation of peripheral venous pressure results from involvement of the right ventricle by the constrictive process. Adequate pericardiolysis of the right ventricle without liberation of the right atrium and entrance of the great veins can relieve peripheral venous hypertension completely. Persistence of peripheral venous hypertension after operation may be the result of right ventricular failure or of residual pericardial scar.

3. The evidence at hand suggests that there is a characteristic right ventricular pressure curve in chronic constrictive pericarditis.

The authors wish to thank Dr. Edward D. Churchill and Dr. Richard H. Sweet for permission to include their patients in the present study. They wish to acknowledge the cooperation of Dr. S. M. Wyman and other members of the Department of Radiology, and the participation of Dr. E. Craige, Dr. J. W. Hurst, Dr. E. G. Dimond, Dr. A. B. Barbour, Dr. T. W. Mattingly, and Dr. J. R. O'Neil. Thanks are due to Miss Ann Murphy for her technical assistance.

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OBSERVATIONS ON THE CIRCULATION IN HIGH SPINAL ANESTHESIA

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SPINAL anesthesia, established clinically by Bier[2] in 1899, has withstood the test of time and remains second only to ether in popularity for major surgical procedures below the level of the diaphragm. The extent of intraspinal block was gradually increased and in 1900 Morton[11] demonstrated that complete body analgesia could be produced by this technique. Operations upon the head under spinal anesthesia were reported by Payne[14] as early as 1901. Because of the frequency of serious complications, however, such extensive spinal conduction block fell into disfavor until used and advocated again by Koster[9] two decades later. He considered the method to be safe and universally applicable. Complications decreased as less toxic anesthetic agents became available, and as the physiology of the anesthetized patient was better understood.

Most recently, anesthesiologists have added to their techniques for permitting painless surgery various methods for making the operation easier and more expeditious for the surgeon. Witness the advent of curare and the numerous curarizing agents. Indeed, the very concomitant of "total" spinal anesthesia which had been feared by most anesthesiologists and surgeons, namely, hypotension, is now advocated as a means of expediting the operation in radical surgery and in seriously ill patients.[7] Since extensive spinal anesthesia is gaining in popularity for surgical analgesia combined with "useful" hypotension, it was deemed advisable to study some of the hemodynamic changes which occur during the hypotension induced by high spinal block.

METHODS

High spinal anesthesia was administered to 35 patients. Twenty-eight of them, 15 men and 13 women, were studied by cardiac catheterization before and during anesthesia. They varied in age between 22 and 63 years, the average being 46. Ten of them were operated upon under the high spinal anesthesia. Most of them had varying degrees of anemia and pulmonary emphysema, but none had azotemia and all but one had normal bromsulfalein excretions. The cardiovascular status was carefully assessed before spinal anesthesia and patients with severe heart disease were not accepted as subjects. Four patients (M. W., W. B., L. M., J. K.) had abnormally low arterial oxygen saturation due to chronic pulmonary emphysema. The renal function was examined by the conventional concentration-dilution test and the phenolsulfonephthalein excretion

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after injection of 6 mg. of the chemical intravenously. These tests were repeated at intervals of three and seven days after spinal anesthesia and surgery. An indwelling urethral catheter was introduced 4 to 6 hours before anesthesia and was allowed to remain in place for at least 12 hours afterward in order to measure the hourly urinary output. The volume and specific gravity of the individual specimens were recorded.

Hemodynamics were studied by means of cardiac catheterization as described in a previous communication.[15] The Fick principle was employed for calculating the cardiac output. The hepatic blood flow was measured as described by Bradley and co-workers.[3] The splanchnic oxygen consumption was calculated according to the method of Myers[13] and the portal hepatic resistance was determined according to Culbertson and co-workers.[6] Oxygen content of the arterial and venous blood specimens was determined by means of a previously standardized Beckman (DU) spectrophotometer. Transduced cardiac and brachial arterial pressures were recorded on the Brush multichannel oscillograph. Pulse volumes and rates of blood flow in the digits were calculated plethysmographically by means of the Grass oscillograph using air transmission to the transducers.

Control data were obtained in a constant temperature room (23 or 24° C.) with the patient lightly sedated (0.1 to 0.2 Gm. of sodium pentobarbital orally) and fasting. High spinal anesthesia was then induced and a surgical operation was performed. Eighteen patients did not undergo operation. These remained in the cardiac catheterization laboratory where the anesthesia was induced, and the experimental data were obtained under conditions identical with those of the control data. In the operative group, preoperative morphine and atropine (0.015 and 0.0004 Gm., respectively) were administered after the control data had been obtained. Another difference between the patients who had operations and those who did not undergo surgery was that in the former (10 cases) light Pentothal Sodium anesthesia was used in order to permit endotracheal intubation and to avoid nausea and vomiting. The level of anesthesia was always to T_3 or higher, as determined in the waking nonoperative patients when 150 to 300 milligrams of procaine dissolved in 4 to 6 c.c. of spinal fluid were injected rapidly into the subarachnoid space with barbotage. An arbitrary period of 15 minutes was allowed for "fixation" of the anesthetic agent. Vasoconstrictor drugs were not used in any case. All patients were placed in head-down position, 5 degrees from the horizontal, 15 minutes after administration of the anesthetic. In 5 of the 10 operative patients spontaneous respiration was permitted. In the other 5 a Pneumatic Balance Resuscitator (P.B.R.), "Burns Model"[12] was used to determine the possible effect of efficient artificial respiration upon the hypotension produced by the anesthesia.

Low spinal anesthesia defined arbitrarily as below the level of T_4 was induced in eighteen patients by injecting 75 to 175 mg. of procaine dissolved in 2 c.c. of spinal fluid. Studies similar to those for the "high spinal" group were made for comparison but the results will not be presented here in detail. An additional 10 patients were studied as controls without spinal anesthesia; 5 with and 5 without the P.B.R.

The experimental data in most instances were obtained 30 and 60 minutes after the administration of the anesthetic. The postoperative care for the patients who had operations was the same as for other hospital patients except that daily twelve-lead electrocardiograms were taken for one week, and renal and hepatic functions were reassessed on the third and seventh days after operation.

RESULTS

A. *General Hemodynamic Changes.*—

The individual data pertinent to 28 patients are tabulated in Tables I to III; average and percentile changes are presented in Table V. Arterial pressures are recorded as systolic, diastolic, and mean; averages are calculated from the mean pressures.

1. *Blood pressure:* The brachial arterial blood pressure dropped in all patients studied. The most marked reductions occurred in the 10 patients who had high spinal anesthesia and were operated upon. Among these, the average reduction, usually maximal at 30 minutes after induction of the anesthesia, was 53 per cent from the basal levels. Those who were not operated upon (18 patients) had an average reduction of 34 per cent from the control blood pressure. These differed from the patients who had operation in that they did not receive morphine and atropine after the control determinations. They did not have Pentothal Sodium and did not have artificial respiration. These drugs may have been responsible for the greater drop in blood pressure in the patients who were operated upon. The operative group also received on the average larger doses of procaine since none in the nonoperative group received over 200 mg. while several in the operative group received 250 and 300 mg. doses.

2. *Heart rate and stroke volume:* Bradycardia developed in proportion to the degree of hypotension in 20 of the 28 patients. In 2 patients (operative) the heart rate increased; in 1 patient (nonoperative) there was a transient increase. In 5, not operated upon, there was virtually no change in heart rate. The average reduction in heart rate among the 28 patients studied under high spinal anesthesia was 11 beats per minute, a reduction of 14 per cent from the control level.

The stroke volume decreased in all but one of the 15 patients in whom this determination was made. The one exception, a patient who had mild congestive failure, showed a slight increase. Among patients who were operated upon, the stroke volume decreased from an average of 57.3 c.c. to 28.3 c.c. These values available in 6 patients who were not operated upon were 57.5 and 33.9, respectively.

3. *Cardiac output and cardiac index:* The cardiac output and cardiac index fell parallel with the reductions in blood pressure. Among the 10 patients who had operations under the high spinal anesthesia, the cardiac output and index fell to 40 per cent of the basal level. These data were obtained in only 6 of the group that were not operated upon, and here the cardiac output and index fell to 72 per cent of the control values.

TABLE I. HEMODYNAMIC DATA OBTAINED IN PATIENTS WHO WERE OPERATED UPON

NAME	AGE	SEX	OPERATION	ANESTHETIC AND LEVEL	BRACHIAL ARTERIAL PRESSURE (MM. HG)			RIGHT ATRIAL PRESSURE (MM. HG)	
					CONTROL	30 MIN.	60 MIN.	CONTROL	60 MIN.
M. W.	62	F	Laparotomy and appendectomy	Pentothal 950 mg., procaine 250 mg.	105/60 84.3	55.5/40 47.2	52.5/36 45.5	1.8/0.0 1.0	0.2/–1.0 –0.8
W. B.	60	M	Revision of burns	Pentothal 750 mg., procaine 300 mg.	99/58 78.6	29/22.5 25.8	31.5/26.7 29.4	1.4/–1.4 0.28	–1.0/–3.0 –2.1
F. F.	27	F	Right oophorectomy, hysterectomy and appendectomy	Pentothal 800 mg., procaine 225 mg.	96/66 79.3	37/27 31.8	38.4/25 28.4	1.6/–0.5 1.08	–1.0/–4.0 –2.8
C. R.	23	M	Right inguinal herniorrhaphy	Pentothal 1000 mg., procaine 250 mg.	102/70 85.0	43.5/39 41.5	58/48 51.5	8.4/4.6 6.7	3.0/–1.0 1.8
H. S.	63	F	Cholecystotomy, choledochostomy and appendectomy	Pentothal 700 mg., procaine 225 mg.	132/60 94.0	36/27 30.6	42/30 38.2	7.4/1.2 3.82	3.0/–2.0 1.1
E. H.*	39	F	Cholecystectomy	Pentothal 850 mg., procaine 150 mg.	112/72 90.0	40/30 33.1			
W. D.*	42	M	Herniorrhaphy; excision necrotic leg ulcer	Pentothal 1000 mg., procaine 150 mg.	118/62 87.0	78/49 60.0			
L. M.*	45	M	Exploratory laparotomy; carcinoma of the pancreas	Pentothal 500 mg., procaine 150 mg.	99/64 80.1	48/37 42.2			
G. L.*	22	F	Herniorrhaphy	Pentothal 300 mg., procaine 200 mg.	112/73 91.1	77/56 65.0			
W. N.*	63	M	Laparotomy and colostomy	Pentothal 250 mg., procaine 150 mg.	144/67 101.4	77/36 52.8	77/41 54.6		

*Those studied with spontaneous respiration.

TABLE I—CONT'D

NAME	PULMONARY ARTERIAL PRESSURE (MM. HG)			HEART RATE			CARDIAC OUTPUT (C.C./MIN.)			CARDIAC INDEX (L./SQ. M./MIN.		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
M. W.	27/12 20.0	20/6 12.5	20.5/6 12.2	88	94	92	6,200	2,500	2,580	3.66	1.48	1.53
W. B.	17.8/6 10.3	11.0/6 8.8	12.2/7 8.9	103	58	60	6,820	865	1,050	3.86	0.49	0.59
F. F.	10/3.5 7.6	7.0/2.5 5.0	7.6/2.0 4.8	81	94	88	4,350	1,470	1,130	3.19	1.08	0.83
C. R.	13.9/7.8 11.2	10.2/5.0 7.4	12.0/6.0 8.7	75	64	62	4,396	2,120	1,605	2.87	1.39	1.05
H. S.	24/71 12.8	16/5.0 11.0	16.8/5.5 11.4	68	50	58	3,950	1,864	1,941	2.92	1.38	1.43
E. H.				70	65		4,518	1,267		2.83	0.79	
W. D.				80	76		5,676	2,806		3.15	1.55	
L. M.				136	111		2,960	1,208		1.90	0.77	
G. L.				88	79		6,697†			3.83†		
W. N.	29.5/14 21.0	24/12 16.4	26/13.5 19.5	61	47	50	3,281	2,844	2,890	1.93	1.67	1.70

†Data not included in averages because they were isolated observations.

TABLE I—CONT'D

NAME	STROKE VOLUME (C.C./MIN.)			OXYGEN CONSUMPTION (C.C./MIN.)			ARTERIAL OXYGEN CAPACITY (VOL. PER CENT)			BRACHIAL ARTERIAL OXYGEN CONTENT (VOL. PER CENT)		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
M. W.	70.6	26.6	28.0	226	134	134	14.92	14.35	14.30	13.34	12.41	12.68
W. B.	66.2	14.9	17.5	218	86.5	104.5	14.89	14.00	14.00	13.35	12.86	13.28
F. F.	53.8	15.7	12.9	156	106	106	14.28	13.35	14.12	12.91	12.36	13.13
C. R.	57.2	33.2	20.5	143	98	98	20.05	18.10	18.20	18.65	16.97	17.06
H. S.	58.0	37.2	33.4	158	108	108	14.28	12.05	12.20	13.30	10.58	10.35
E. H.	64.5	19.5		172	95		17.99	15.60		16.60	15.00	
W. D.	71.0	37.0		256	188		17.88	17.60		16.70	16.40	
L. M.	21.0	12.0		127	55		17.00	16.80		15.10	15.30	
G. L.	75.0†			233	186		14.00	13.50		13.10	12.60	
W. N.	53.7	60.5	57.8	190	192	196	20.20	19.42	19.42	18.91	18.16	18.12

TABLE I—CONT'D

NAME	PULMONARY ARTERIAL OXYGEN CONTENT (VOL. PER CENT)			BRACHIAL ARTERIAL PULMONARY ARTERIAL OXYGEN DIFFERENCE (VOL. PER CENT)			ARTERIAL OXYGEN SATURATION			LEFT VENTRICULAR WORK (KG. M. /MIN.)		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
M. W.	9.70	7.05	7.48	3.64	5.36	5.20	89.3	86.3	88.6	7.05	1.60	1.59
W. B.	10.15	3.12	3.83	3.20	9.74	9.45	89.6	91.8	94.8	7.24	0.30	0.42
F. F.	0.32	5.14	3.51	3.59	7.22	9.52	90.4	92.5	93.0	4.66	0.63	0.42
C. R.	15.42	12.42	11.58	3.23	4.55	5.48	93.0	93.7	93.7	5.04	1.19	1.11
H. S.	9.30	4.60	4.84	4.00	5.78	5.51	93.1	87.8	84.0	5.02	0.77	1.00
E. H.	12.80	7.50		3.80	7.50		92.5	96.0		5.49	0.56	
W. D.	12.20	9.70		3.50	6.70		93.4	93.1		6.67	2.27	
L. M.	10.10	7.80		4.90	7.50		89.0	91.0		3.19	0.68	
G. L.	9.64†			3.46†			93.5	93.3		8.23†		
W. N.	13.12	11.41	11.34	5.79	6.75	6.78	93.6	93.5	93.3	5.84	0.20	0.21

†Data not included in average because they were isolated observations.

TABLE II. HEMODYNAMIC DATA OBTAINED IN PATIENTS WHO WERE NOT OPERATED UPON

TABLE II. HEMODYNAMIC DATA OBTAINED IN PATIENTS WHO WERE NOT OPERATED UPON

NAME	AGE	SEX	DIAGNOSIS	ANESTHETIC AND LEVEL	BRACHIAL ARTERIAL PRESSURE (MM. HG)			RIGHT ATRIAL PRESSURE (MM. HG)	
					CONTROL	30 MIN.	60 MIN.	CONTROL	60 MIN.
J. K.	56	M	Senility	Procaine 150 mg., T_3	132/78 102	84/58 73	102/60 80.4	6.1/3.0 4.9	5.9/2.0 4.3
F. B.	43	F	Obesity	Procaine 175 mg., T_2	138/83 105		68/37.5 52	8.0/–2.5 4.4	2.0/–1.0 0.4
M. G.	41	F	Abdominal mass of unknown etiology	Procaine 150 mg., T_1	113/69 93	67/45 55.8	87/60 73.2	3.0/1.5 2.1	–2.0/–2.5 –1.2
F. D.	46	F	Paroxysmal hypertension	Procaine 150 mg., T_1 T_2	114/66 91	54/36 43.8	66/42 53.8	5.2/2.4 3.47	4.2/1.6 3.1
T. G.	60	M	Drug reaction	Procaine 175 mg., T_1 T_2	145/71 101.4	63/36 47.9	75/41 56.7	10.5/1.8 4.8	4.7/1.2 2.6
H. W.*	39	F	Korsakow psychosis	Procaine 160 mg., T_3	150/88 114.6	83/53 61.5	85/56 67.7	8/1.5 4.1	4/0.5 2.1
W. R.*	57	M	No disease	Procaine 160 mg., T_2	94/65 80.4	72/44 60	86/55 73.8		
J. C.*	31	M	Peptic ulcer	Procaine 125 mg., T_2	107/68 88.8	84/55 72.6	79/54 67.8	3.5/1.5 2.8	2.5/1 1.9
P. P.*	45	M	Alcoholic neuropathy	Procaine 200 mg., T_2	105/61 81	76/54 63.6	59/42 46.8	5/2.7 3.6	2/0 0.9
C. P.*	59	M	Psychoneurosis	Procaine 175 mg., T_2	98/66 82.2	67/50 58.4	66/50 60.6	–0.5/–2.2 –1.2	–1/–3 –2.2

TABLE II—CONT'D

NAME	PULMONARY ARTERIAL PRESSURE (MM. HG)			HEART RATE			CARDIAC OUTPUT (C.C./MIN.)			CARDIAC INDEX (L./SQ. M./MIN.)		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
J. K.	28.7/9.5 18.7	22/8.5 16.8	25/10 17.5	81	77	79	5,204	3,876	4,365	2.79	2.08	2.34
F. B.	21.5/11 16.8		16.5/7.7 11.1	83		56	5,718		3,060	3.0		1.60
M. G.	16.5/6.5 11.5	9.5/2.5 6.3	10/2.5 6.3	87	86	83	3,427	2,360	2,707	2.46	1.69	1.94
F. D.	15.5/8.5 12.5	10.1/5.5 7.9	11.5/6.8 8.4	82	76	81	3,873	3,438	4,230	2.76	2.45	3.02
T. G.	17.5/9.7 14.8	12.5/4.7 4.7	13.5/6 10.2	80	65	60	5,315	3,315	4,449	2.90	1.80	2.43
H. W.*				88	75	71						
W. R.*				68	67	62	4,127	2,976	3,979	2.80	2.02	2.70
J. C.*				81	83	77						
P. P.*				71	68	71						
C. P.*				91	75	77						

*These patients were studied primarily to determine their hepatic blood flow, hence the paucity of other data.

TABLE II—CONT'D

NAME	STROKE VOLUME (C.C./MIN.)			OXYGEN CONSUMPTION (C.C./MIN.)			ARTERIAL OXYGEN CAPACITY (VOL. PER CENT)			BRACHIAL ARTERIAL OXYGEN CONTENT (VOL. PER CENT)		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
J. K.	64.2	50.2	55.2	218	195	203	13.78	13.15	12.75	12.36	11.58	11.35
F. B.	68.6		54.6	195		172	15.85		15.80	14.38		14.28
M. G.	39.3	27.4	32.6	134	122	127	15.63	15.63	15.48	14.30	14.65	14.35
F. D.	47.2	45.2	52.2	153	155	176	15.09	15.09	15.09	13.80	13.68	13.73
T. G.	66.0	51.0	74.0	219	184	198	11.80	11.41	11.41	10.84	10.26	10.30
H. W.							16.88	15.82	15.41	15.70	14.55	14.20
W. R.				175	165	181	16.25	15.20	15.20	15.34	14.65	14.70
J. C.							19.27	18.65	18.65	18.17	17.58	17.57
P. P.							17.80	17.49	17.49	16.59	16.68	16.61
C. P.							16.06	15.82	15.82	14.94	14.58	14.74

TABLE II—CONT'D

NAME	PULMONARY ARTERIAL OXYGEN CONTENT (VOL. PER CENT)			BRACHIAL ARTERIAL, PULMONARY ARTERIAL OXYGEN DIFFERENCE (VOL. PER CENT)			ARTERIAL OXYGEN SATURATION			LEFT VENTRICULAR WORK (KG. M./MIN.)		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
J. K.	8.21	6.55	6.70	4.15	5.03	4.65	89.6	88.0	89.0	7.17	3.80	4.73
F. B.	10.97		8.65	3.41		5.62	90.7		90.3	8.10		2.14
M. G.	10.38	9.46	9.66	3.91	5.19	4.69	94.1	93.7	92.7	4.30	1.78	2.67
F. D.	9.85	9.26	9.57	3.95	4.42	4.16	91.4	90.6	90.9	5.73	2.08	3.02
T. G.	6.72	4.71	5.85	4.12	5.55	4.45	91.8	90.0	90.2	7.28	2.14	3.40
H. W.							93.0	92.2	92.1			
W. R.	11.10	9.14	10.15	4.24	5.51	4.55	94.4	96.3	96.6	4.48	2.41	3.96
J. C.							94.2	94.2	94.2			
P. P.							93.2	94.8	94.7			
C. P.							92.8	92.1	93.1			

TABLE III. HEMODYNAMIC DATA OBTAINED IN PATIENTS WHO WERE NOT OPERATED UPON AND WERE STUDIED PRIMARILY TO DETERMINE CORONARY AND CEREBRAL BLOOD FLOWS

NAME	AGE	SEX	DIAGNOSIS	ANESTHETIC AND LEVEL	BRACHIAL ARTERIAL PRESSURE (MM. HG)			RIGHT ATRIAL PRESSURE (MM. HG)	
					CONTROL	30 MIN.	60 MIN.	CONTROL	60 MIN.
E. F.	61	M	Resolved bronchopneumonia and hypertension	Procaine 200 mg., T_1	225/105 156.3	47/29 36.6		4/0.12 2.5	1.4
M. C.	54	F	Obesity, hypertension	Procaine 160 mg., C_3	176/87 122.4	85/48 60			
M. K.	55	M	Psychosis	Procaine 200 mg., T_3	168/83 122.8	59/40 54.4		3.8	1.2
A. B.	46	F	Menopausal syndrome	Procaine 150 mg., T_3	125/74 97.6	89/54 72			
G. S.	39	F	Diabetes and chronic cholecystitis	Procaine 170 mg., T_1	137/90 114	93/60 76.8			
E. T.	36	F	Hypertension	Procaine 175 mg., T_1	195/120	129/86			
S. K.	42	M	Central nervous system syphilis, treated	Procaine 175 mg., T_2	113/65 89.4	75/48 60.0			
M. S.	33	M	Delirium tremens, cured	Procaine 150 mg., T_3	123/71 91.2	80/41 56.4			

TABLE III—CONT'D

NAME	HEART RATE			ARTERIAL OXYGEN CAPACITY (VOL. PER CENT)			BRACHIAL ARTERIAL OXYGEN CONTENT (VOL. PER CENT)			ARTERIAL OXYGEN SATURATION		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
E. F.	79	48		16.81	16.30		15.31	14.45		90.9	88.6	
M. C.	72	40		18.38	17.49		17.00	16.35		92.4	93.3	
M. K.	71	71		15.40	15.13		13.90	13.95		90.3	92.3	
A. B.	52	44		17.60	16.05		16.48	14.03		93.6	87.2	
G. S.	83	56		17.44	16.25		16.08	14.59		92.2	89.8	
E. T.	81	58		16.40	16.40		15.40	13.60		93.9	93.1	
S. K.	71	68		18.18	17.16		17.22	16.24		94.7	92.5	
M. S.	79	79		21.20	20.40		20.13	19.23		95.0	94.2	

TABLE IV. HEMODYNAMIC DATA IN PATIENTS WHO WERE NOT OPERATED UPON AND WERE STUDIED PRIMARILY TO DETERMINE SPLANCHNIC BLOOD FLOW

NAME	AGE	DIAGNOSIS	ANESTHETIC AND LEVEL	BRACHIAL ARTERIAL PRESSURE (MM. HG)			ESTIMATED HEPATIC BLOOD FLOW (C.C./SQ. M./MIN.)		
				CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
H. W.	39	Korsakow psychosis	Procaine 160 mg., T_3	150/88 114.6	83/53 61.5	85/56 67.7	1,085	910	919
W. R.	57	No disease	Procaine 160 mg., T_2	94/65 80.4	72/44 60.0	86/55 73.8	744	511	656
J. C.	31	Peptic ulcer	Procaine 125 mg., T_2	107/68 88.8	84/55 72.6	79/54 67.8	1,282	934	647
P. P.	45	Alcoholic neuropathy	Procaine 200 mg., T_2	105/61 81.0	76/54 63.6	59/42 46.8	493	303	295
C. P.	59	Psychoneurosis	Procaine 175 mg., T_2	98/66 88.2	67/50 58.4	66/50 60.6	810	504	432
Average	46			89.4	63.2	63.3	883	632	590
Per cent change					−27.0	−27.0		−28.4	−33.1

TABLE IV—CONT'D

NAME	BRACHIAL ARTERIAL HEPATIC VENOUS OXYGEN DIFFERENCE (VOL. PER CENT)			HEPATIC VENOUS OXYGEN CONTENT (VOL. PER CENT)			SPLANCHNIC OXYGEN CONSUMPTION (C.C./SQ. M./MIN.)			HEPATIC PORTAL RESISTANCE (MM. HG/C.C./SEC./SQ. M.)		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
H. W.	5.52	8.42	7.18	10.18	6.13	7.02	60	76	66	6.4	4.1	4.4
W. R.	4.80	7.22	6.10	10.54	7.43	8.60	36	37	40	6.5	7.1	6.8
J. C.	4.59	6.41	7.23	13.58	11.17	10.34	59	60	47	4.1	4.7	6.3
P. P.	5.10	7.50	8.63	11.49	9.18	7.98	25	23	25	9.9	12.5	9.5
C. P.	5.46	9.98	9.22	9.48	4.60	5.52	44	50	40	6.1	7.0	8.4
Average	5.09	7.90	7.67	11.05	7.70	7.89	45	49	44	6.6	7.1	7.1
Per cent change		+35.5	+33.6		−30.3	−28.6		+8.8	−2.2		+7.0	+7.0

TABLE V. AVERAGES AND PERCENTILE CHANGES OF THE HEMODYNAMIC DATA PRESENTED (INDIVIDUAL GROUPS)

	MEAN BRACHIAL ARTERIAL PRESSURE (MM. HG)			RIGHT ATRIAL MEAN PRESSURE (MM. HG)		PULMONARY ARTERIAL MEAN PRESSURE (MM. HG)		
	CONTROL	30 MIN.	60 MIN.	CONTROL	60 MIN.	CONTROL	30 MIN.	60 MIN.
Operative group, artificial respiration (5 cases)								
Average	84.2	35.4	38.6	2.58	0.56	12.4	8.94	9.20
Per cent change		−58%	−54%		−122%		−28%	−26%
Operative group, spontaneous respiration (5 cases)								
Average	89.9	50.6						
Per cent change		−43%						
Total operative group (10 cases)								
Average	87.1	43.0	41.2	2.58	0.56	13.8	10.2	10.9
Per cent change		−50%	−53%		−122%		−26%	−21%
Nonoperative group (18 cases)								
Average	95.4	62.5	63.3	3.2	1.36	14.9	8.9	10.7
Per cent change		−34%	−33%		57%		−40%	−28%
Total group (28 cases)								
Average	98.6	55.3	55.0	3.1	0.73	14.3	9.7	10.8
Per cent change		−44%	−44%		−76%		−32%	−24%

TABLE V—CONT'D

	HEART RATE			CARDIAC OUTPUT (C.C./MIN.)			CARDIAC INDEX (L./SQ. M./MIN.)		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
Operative group, artificial respiration (5 cases)									
Average	83	72	72	5,143	1,764	1,661	3.30	1.16	1.09
Per cent change		−13%	−13%		−66%	−68%		−65%	−67%
Operative group, spontaneous respiration (5 cases)									
Average	87	76		4,109	2,031		2.45	1.19	
Per cent change		−13%			−50%			−51%	
Total operative group (10 cases)									
Average	85	74	68	4,683	1,883	1,866	2.92	1.18	1.19
Per cent change		−13%	−20%		−60%	−58%		−60%	−58%
Nonoperative group (18 cases)									
Average	77	67	72	4,611	3,193	3,798	2.78	2.00	2.33
Per cent change		−13%	−6.5%		−30%	−18%		−28%	−16%
Total group (28 cases)									
Average	80	69	70	4,654	2,343	2,832	2.86	1.47	1.80
Per cent change		−14%	−12%		−50%	−39%		−49%	−37%

TABLE V—CONT'D

	STROKE VOLUME (C.C./MIN.)			OXYGEN CONSUMPTION (C.C./MIN.)			OXYGEN CAPACITY (VOL. PER CENT)		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
Operative group, artificial respiration (5 cases)									
Average	61.2	25.5	22.5	180.2	106.4	110.1	15.68	14.37	14.56
Per cent change		−58%	−63%		−41%	−39%		−8%	−7%
Operative group, spontaneous respiration (5 cases)									
Average	52.5	32.2		196	143		17.41	16.58	
Per cent change		−39%			−27%			−4.7%	
Total operative group (10 cases)									
Average	57.3	28.3	28.3	188	125	124	16.54	15.47	15.37
Per cent change		−51%	−51%		−33%	−33%		−6.4%	−7%
Nonoperative group (18 cases)									
Average	57.6	43.6	55.5	182	164	176	16.65	16.08	15.31
Per cent change		−24%	−3%		−10%	−3%		−3.4%	−8%
Total group (28 cases)									
Average	57.5	33.9	41.9	186	138	150	16.61	15.86	15.33
Per cent change		−41%	−27%		−26%	−19%		−4.4%	−7.7%

TABLE V—CONT'D

	BRACHIAL ARTERIAL OXYGEN CONTENT (VOL. PER CENT)			PULMONARY ARTERIAL OXYGEN CONTENT (VOL. PER CENT)			BRACHIAL ARTERIAL, PULMONARY ARTERIAL OXYGEN DIFFERENCE (VOL. PER CENT)		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
Operative group, artificial respiration (5 cases)									
Average	14.31	13.04	13.30	10.78	6.47	6.25	3.55	6.53	7.03
Per cent change		−8%	−7%		−40%	−42%		+46%	+49%
Operative group, spontaneous respiration (5 cases)									
Average	16.08	15.49		12.05	9.10		4.75	7.11	
Per cent change		−3.7%			−24%			+33%	
Total operative group (10 cases)									
Average	15.19	14.26	14.10	11.34	7.64	7.09	4.07	6.79	6.99
Per cent change		−6.1%	−7.1%		−33%	−37%		+40%	+42%
Nonoperative group (18 cases)									
Average	15.44	14.74	14.18	9.54	7.82	8.43	3.96	5.14	4.68
Per cent change		−4.5%	−8.1%		−18%	−12%		+23%	+15%
Total group (28 cases)									
Average	15.35	14.68	14.15	10.62	7.70	7.76	4.03	6.20	5.84
Per cent change		−4.3%	−7.8%		−27%	−26%		+35%	+31%

TABLE V—CONT'D

	ARTERIAL SATURATION			LEFT VENTRICULAR WORK (KG. M./MIN.)		
	CONTROL	30 MIN.	60 MIN.	CONTROL	30 MIN.	60 MIN.
Operative group, artificial respiration (5 cases)						
Average	91.1	90.4	90.8	5.80	0.90	0.91
Per cent change					−84%	−84%
Operative group, spontaneous respiration (5 cases)						
Average	92.4	93.4		5.25	0.93	
Per cent change					−82%	
Total operative group (10 cases)						
Average	91.8	91.9	91.2	5.58	0.91	0.79
Per cent change					−83%	−85%
Nonoperative group (18 cases)						
Average	92.7	91.8	92.4	6.18	2.44	3.32
Per cent change					−60%	−46%
Total group (28 cases)						
Average	92.3	91.9	92.0	5.81	1.45	2.05
Per cent change					−75%	−65%

4. *Right auricular and pulmonary arterial pressures:* All patients studied showed a great reduction in both the right auricular and the pulmonary arterial pressures. The right auricular pressure in the patients who had surgery under high spinal anesthesia showed average reductions of 122 per cent from the control levels. The pulmonary arterial pressure dropped an average of 26 per cent. The patients who were not operated upon showed a drop of 57 per cent from the basal right auricular pressure and a drop of 40 per cent from the basal pulmonary arterial pressure.

5. *Oxygen consumption:* High spinal anesthesia produced a decrease in the oxygen consumption of all patients studied. Among those who had surgery performed (10 cases) under high spinal and Pentothal Sodium anesthesia the oxygen consumption fell in all but one (in whom there was virtually no change) and it is noteworthy that this patient had the least amount of Pentothal Sodium for supplemental anesthesia (250 mg.). The average drop among the 10 patients operated upon was 33 per cent; among those not operated upon (6 cases), the decrease in oxygen consumption was only 10 per cent.

6. *Arteriovenous oxygen difference:* The difference between the oxygen contents of brachial and pulmonary arterial blood increased in all the patients in whom the data are available (15 cases). The greatest change occurred in those who had operations. Among these the oxygen difference increased to 6.79 (average) from 4.07 (average) volumes per cent. The changes were primarily the result of significant reductions in the pulmonary arterial oxygen contents which exceeded the constant but slight reductions observed in the oxygen content of the brachial arterial blood in the same patients. In those patients not operated upon, the brachial pulmonary arteriovenous oxygen difference increased from 4.03 to 6.20 volumes per cent.

7. *Arterial oxygen saturation and capacity:* The oxygen saturation of arterial blood was not significantly altered by high spinal anesthesia except in

two of the patients who were operated upon and for both of whom artificial respiration was used. In retrospect, the line pressures for the Pneumatic Balance Resuscitator in both cases were inadequate. The mechanics of pulmonary ventilation were far more important in determining arterial oxygen saturation than any possible direct effect of the anesthetic agents upon the blood.

The arterial oxygen capacity fell slightly in all groups of patients studied. This was attributed to a slight fall in the hematocrit level during the tests. The average fall in the hematocrit level among 10 subjects who had high spinal anesthesia was 3.3 per cent. The possible mechanisms to account for this slight hemodilution and decreased oxygen capacity were not tested.

8. *Calculated left ventricular work:* The calculated left ventricular work was reduced in all patients for whom this determination was made (15 cases), decreasing an average of 75 per cent from the control value. In those operated upon (9 cases), the left ventricular work dropped 85 per cent; in the nonoperative group (6 cases) the value fell 60 per cent from the control levels.

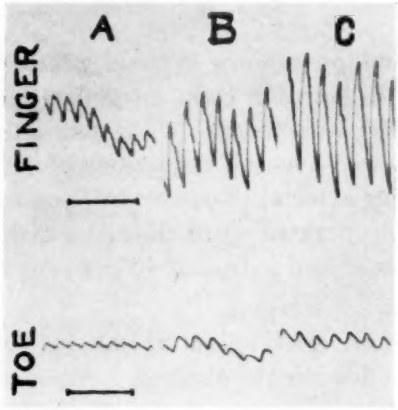

Fig. 1.—Records of the pulse volume (patient T. G., age 60 years) obtained with the Grass oscillograph adapted for plethysmography. Upper records: index finger. *A:* before anesthesia (0.0025 ml. per 5 ml. of part); *B:* 30 minutes after induction of anesthesia (0.0094 ml. per 5 ml. of part); *C:* 60 minutes after induction of anesthesia (0.013 ml. per 5 ml. of part). Lower record: second toe. *A:* before anesthesia (0.0035 ml. per 5 ml. of part); *B:* 30 minutes after induction of anesthesia (0.0075 ml. per 5 ml. of part); *C:* 60 minutes after induction of anesthesia (0.0075 ml. per 5 ml. of part).

9. *Peripheral blood flow:* The pulse volume and the rate of blood flow increased in the digits of the hands and feet under high spinal anesthesia despite the hypotension and the decreased cardiac output (Figs. 1 and 2). If the mean blood pressure, however, fell to very low levels (below 30 mm. Hg), the pulse volumes and rates of blood flow decreased to below the control levels. In 10 patients, the increase in digital blood flow during high spinal anesthesia averaged 244 per cent.

B. *Effects Upon Hepatic Circulation.*—The data pertinent to splanchnic flow studies are presented in Table IV.

The hepatic blood flow was reduced under high spinal anesthesia in all of five patients studied. None was operated upon. The decrease amounted to 33.1 per cent from the control blood flow. The reduced hepatic blood flow was accompanied by an increased difference between the oxygen content of brachial

arterial and of hepatic venous samples of blood, and this difference was 35.5 per cent greater than it was in the control specimens of blood. The splanchnic oxygen consumption was not significantly altered by the spinal anesthesia, nor was the portal hepatic resistance changed significantly.

C. *Liver and Kidney Function.*—

Only one of the 10 operative patients studied under high spinal anesthesia had an abnormal preoperative bromsulfalein retention (28 per cent) 60 minutes after the injection of 5 mg. per kilogram of body weight. Among those who received high spinal anesthesia and were operated upon, 8 out of 9 previously normal subjects showed abnormal bromsulfalein retention 3 days postoperatively and 5 of these were still abnormal 7 days postoperatively. The retention increased further in the patients who had an abnormal retention preoperatively. Only 1 patient, previously normal, showed no effect upon the bromsulfalein retention after the anesthesia. Only 1 of 11 patients with normal preoperative bromsulfalein excretions operated upon and studied under low spinal anesthesia showed abnormal bromsulfalein retention 3 days postoperatively.

Renal function as measured by the concentration-dilution tests and by the intravenous phenolsulfonephthalein tests was within normal limits preoperatively in all patients studied, and there was no significant change on the third and seventh postoperative days.

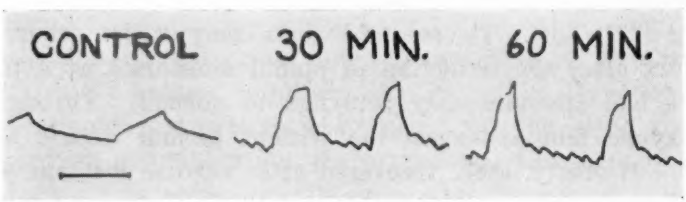

Fig. 2.—Records of rates of blood flow in finger tip (patient H. W., age 39 years) before and during high spinal anesthesia. Control: 0.62 ml. per minute; at 30 minutes: 3.2 ml. per minute; at 60 minutes: 3.5 ml. per minute. All values corrected to 10 ml. of part. Records made by venous occlusion produced by inflating a cuff about the base of the digit.

There was a consistent reduction in the rate of urinary flow during all forms of spinal anesthesia whether high or low. In no case was there an increased flow of urine, as compared with the preanesthesia rate, and in patients who had high spinal anesthesia there was usually complete cessation of urinary flow during the period of greatest hypotension. The average preoperative flow of urine in the patients who received high spinal anesthesia was 1.99 c.c. per minute. It fell to 0.09 c.c. per minute (average) during the period of anesthesia.

D. *Clinical Observations.*—Nausea was common among conscious patients under high spinal anesthesia, but was always alleviated by the inhalation of 100 per cent oxygen for a few minutes. Vomiting occurred in only 2 of the 18 subjects who did not have supplemental Pentothal Sodium anesthesia. In only 1 subject was it necessary to postpone the 30-minute determination because of vomiting. A patient, 61 years of age, had Cheyne-Stokes respiration for 20 minutes. These symptoms were not observed in patients who were operated upon and who had Pentothal Sodium in addition to the spinal anesthesia.

In the waking subjects, when high levels of anesthesia were achieved, apprehension was commonly observed and in one patient in whom total body anesthesia was produced, a feeling of impending death was experienced. Some subjects, however, were calm and unconcerned even with sensory levels of anesthesia as high as C_3 and with mean blood pressures as low as 36 mm. Hg. Patients yawned repeatedly and felt sleepy when the upper thoracic segments were paralyzed. Respiration became diaphragmatic and its rate increased transiently when the level of anesthesia passed beyond T_4 but soon returned to normal or became slower than before the anesthesia. Artificial respiration was necessary for 30 minutes in 1 patient during surgery. Postanesthesia headache was observed in only 1 case.

Very little bleeding was encountered during surgery in the patients under high spinal anesthesia. During a cholecystectomy, for instance, it was necessary to ligate only the cystic artery. In every case, relaxation was excellent and there was general agreement that surgery was facilitated.

Untoward effects were observed only in the patients who were operated upon. One of them (E. H.) died suddenly 26 hours after cholecystectomy. This patient had required artificial respiration for 30 minutes during surgery. On the morning after operation she was ambulatory and free of complaints. Six hours later she suddenly collapsed and died. Thorough post-mortem examination could detect no signs of ischemic effects in the brain, myocardium, kidneys, or liver. The cause of death was massive atelectasis of both lungs, predominantly of the left. The second serious complication occurred in another patient, 2 hours after the induction of spinal anesthesia at a time when the blood pressure had spontaneously returned to normal. Through a technical problem in oxygen administration the patient became anoxic and developed cardiac arrest. He fortunately recovered after cardiac massage and the establishment of adequate pulmonary ventilation. While it may not be fair to attribute this complication directly to high spinal anesthesia it is important to record it to emphasize the importance of maintaining adequate aeration in this as well as in other types of anesthesia.

DISCUSSION

The data presented in this report demonstrate that high spinal anesthesia above the level of T_4 is accompanied by dramatic changes in the circulation. These changes are thought to be primarily the result of paralysis of preganglionic vasomotor fibers as they traverse the anterior roots of the spinal nerves. It is interesting that patients under low spinal anesthesia exhibit circulatory changes which, with one exception, differ in degree only from those observed under high spinal anesthesia. Thus, when the studies described above were done in 18 patients in whom the spinal block reached no higher than the lower thoracic segments, the only qualitative difference was that the rate of blood flow in the fingers decreased as the result of compensatory vasoconstriction, whereas it increased in the patients who had high spinal anesthesia.

In evaluating the safety of high spinal anesthesia, it is important to assess the physiologic effects of the circulatory changes described. The degrees to

which the blood pressure, cardiac output, and stroke volume are decreased are alarming when taken per se. Griffiths and Gillies[7] have emphasized that the circulation through the tissues may not be impaired by the drop in blood pressure because the arteriolar dilatation makes unnecessary the high prearteriolar blood pressure which exists normally. This was clearly demonstrable in the skin so long as the mean blood pressure remained above 30 mm. Hg. Observations on the circulation in striated muscle were not made, but it is reasonable to suppose that circulatory changes might occur there in the same direction as those in the skin.

One must feel less confident, however, regarding the circulation through the viscera. The rate of blood flow through the liver is decreased. Also, as measured by the ability of the liver to clear bromsulfalein, the function of that organ was impaired in all but one of the patients who had high spinal anesthesia. While no evidence of renal impairment could be detected 3 and 7 days postoperatively by the tests employed, it can be assumed that during the period of hypotension the circulation through the kidney must have been decreased. Both the volume and the specific gravity of the urine excreted during the period of hypotension decreased. These observations are in accord with those of others [1, 4, 5, 8] who showed that the renal blood flow is markedly decreased during deep cyclopropane, thiopental, ether, and high spinal anesthesia. Renal blood flow could not be studied during the period of anesthesia in our patients because of the anuria.

Work still in progress suggests that the rate of blood flow in the coronary bed of the heart is decreased significantly during the period of hypotension. Unlike the liver which extracts more oxygen from the blood passing through it during the period of hypotension, the extraction of oxygen by the heart does not increase during high spinal anesthesia so that its rate of oxygen utilization decreases along with the decrease in the rate of coronary blood flow. In addition, no significant changes could be detected in the electrocardiograms during the period of anesthesia and hypotension. In two of the patients operated upon (W. B. and H. S.) there was an inversion of the T waves in leads V_3 and V_4 on the third postoperative day. The records were normal again in both patients by the next day. The results of studies on the cerebral circulation have so far been too few and too variable to warrant conclusions.

With the exception of the skin (and possibly the muscles), therefore, one may conclude that the circulation through other organs is probably decreased during the hypotension resulting from high spinal anesthesia. The argument, then, that reduction of arteriolar resistance balances the reduction in the head of pressure does not hold for the kidneys, liver, and heart. It may be important to emphasize that while the coronary circulation may decrease during the hypotension, the estimated work of the heart also decreases and so does its rate of oxygen consumption. It does not necessarily follow, however, that the decreased cardiac work and oxygen consumption are sufficient to balance the decreased circulation through the myocardium even though the electrocardiogram shows no abnormality during the period of hypotension.

Thirty-five patients, 28 of whom were studied in the laboratory, have received effective high spinal anesthesia at City Hospital. Thirteen* of them were operated upon. The 2 serious complications occurred among these 13. One (cardiac arrest) cannot be attributed directly to the spinal block but rather to failure to maintain adequate pulmonary aeration. The patient, who died of massive collapse of the lungs, showed no histologic findings to suggest effects of ischemia or anoxia which might have resulted from hypotension. Nevertheless, it is reasonable to ascribe her death to this form of anesthesia resulting either from the hemodynamic effects of vasomotor paralysis or from possible untoward effects of respiratory paralysis for which artificial respiration was required for thirty minutes. As Griffiths and Gillies have emphasized,[7] if one is to use this form of anesthesia it is imperative to be familiar with the physiology of this type of hypotension and to be absolutely certain that pulmonary ventilation is not impaired. Their results with high spinal anesthesia have been excellent when attention was paid to ventilation and adequate circulation for the brain. Indeed, these points were emphasized by Lord Lister[10] nearly a century ago and apply to any kind of anesthesia. They make the use of high spinal anesthesia safe only in hands experienced in the selection of patients and their management during this form of anesthesia.

SUMMARY AND CONCLUSIONS

1. Observations are reported from a study of 35 patients receiving high spinal anesthesia, in 28 of whom hemodynamic data were obtained.

2. The systemic blood pressure, the cardiac output, the stroke volume, the work of the heart, and the right atrial and pulmonary artery pressures decrease.

3. The oxygen desaturation of blood reaching the right side of the heart is increased.

4. The circulation in the skin is increased so long as the mean systemic blood pressure does not fall below 30 mm. Hg.

5. Direct and indirect evidence indicates that the circulation in the liver, kidneys, and heart is decreased during the period of hypotension.

6. The work of the heart and its rate of oxygen consumption are decreased during the hypotension and the question is raised whether this decreased requirement of the heart can compensate for the decreased circulation through it.

7. Two serious complications among the 13 patients operated upon are reported. One of them is not attributable to the spinal anesthesia directly while the other may be.

8. Further studies on the effects of high spinal block upon the circulation through the viscera and brain are needed before the safety of this form of anesthesia can be finally assessed.

9. When high spinal anesthesia is used, the anesthetist must be familiar with the physiology of this type of hypotension and must take every precaution to maintain adequate pulmonary ventilation.

The authors are indebted to Miss Gladys Heckman, R.N., and Miss Hanna Janouskovec, R.N., for their assistance in this work.

*Hemodynamic studies were done in only 10 of these (Table I).

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DISCUSSION

MR. D. H. PATEY.—In Scotland and England, this method of low blood pressure has been used as an aid in hemostasis. I would just like to tell you of one complication that happened to me, not from this particular method but from use of the hexamethonium compound. In a number of cases in Middlesex this low blood pressure method has been used. We thought it was innocuous and then I had a case, carcinoma of the breast, which technically, surgically, and apparently anesthetically was uneventful, in which the patient's blood pressure was kept at a low level by the use of hexamethonium compound. The patient was, after operation, blind in one eye. The patient was seen by Dr. Goldsmith, our ophthalmologist, and he had never seen anything comparable before. He called in Sir Duke Elder who said that he had not seen blindness in one eye, or in both eyes, from this low blood pressure technique before, but on inquiries, he heard of two cases that had had cerebral catastrophes following this low blood pressure technique. Our feeling at Middlesex is that this low blood pressure technique ought only to be used in a type of case in which there is something tremendously to be gained in the way of hemostasis; such as, being able to operate on some cerebral or vascular condition that perhaps otherwise would not have been operable. If the method does not provide some outstanding advantage, such as converting an inoperable into an operable case, one should be very, very careful indeed in using these low blood pressure techniques during anesthesia until this problem is solved.

SOME EFFECTS UPON THE LIVER OF COMPLETE ARTERIALIZATION OF ITS BLOOD SUPPLY

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THE general trend of operative procedures designed to relieve the effects of portal hypertension has been to decrease the total blood supply to that organ. Since the function of every organ is dependent upon its blood supply, these operations, while conceivably solving the immediate difficulty, must in the long run do so at the price of liver function. As it has been shown repeatedly since Eck's original paper that diversion of the portal blood flow results in atrophy of the liver, theoretically one should increase the flow to a diseased organ to aid regeneration. The following experiment represents an attempt to increase the blood supply to the liver while avoiding the secondary effects of portal hypertension.

Mongrel dogs kept on a standard stock diet were operated upon using intravenous Nembutal anesthesia with positive pressure supplied through an intratracheal tube. The right chest was opened through the bed of the tenth rib and the incision extended through the diaphragm into the abdomen. The portal vein was identified and dissected free. It was then cut across 1 cm. from the hilum of the liver and an end-to-side anastomosis was constructed between the distal portal vein and the vena cava. Next, the jugular vein, having been previously removed, was anastomosed as a free graft to the proximal end of the portal vein. The graft was pulled through the posterolateral corner of the diaphragm. The aorta was freed up in this area and occluded between two Blalock clamps. The free end of the vein graft was anastomosed to the side of the aorta, the opening being about 3 or 4 mm. in diameter. All clamps were removed. If no bleeding occurred, the diaphragm, chest wall, and abdomen were closed after re-expanding the lung. Fig. 1 shows a drawing of the graft in place.

In the last 25 operations there have been 3 deaths. One animal died on the fourth day from hemorrhagic pneumonia. Two other animals died within 48 hours from portal venous obstruction due to angulation at the site of the Eck fistula. All animals were given penicillin, 100,000 units only.

After about 7 days the animals which survived the operation appeared clinically well. In 12 animals a loud murmur could be heard under the right costal margin. The murmur gradually diminished in intensity.

Fig. 2 is an aortic angiogram 6 weeks postoperatively. The irregular vein graft can be seen coming off the aorta just above the smaller smooth celiac axis.

If the aortic opening is too large, aneurysmal dilation of the portal vein occurs. In dog 15, which died 14 weeks after operation, the portal vein at the hilum was thickened and had the appearance of an artery. It measured 2.3 cm. in diameter. The dog at termination of the experiment weighed 15½ kg. His liver weighed 1,045 Gm., about a threefold increase in size.

Read at the meeting of the Society of University Surgeons, Baltimore, Md., Feb. 7-9, 1952.

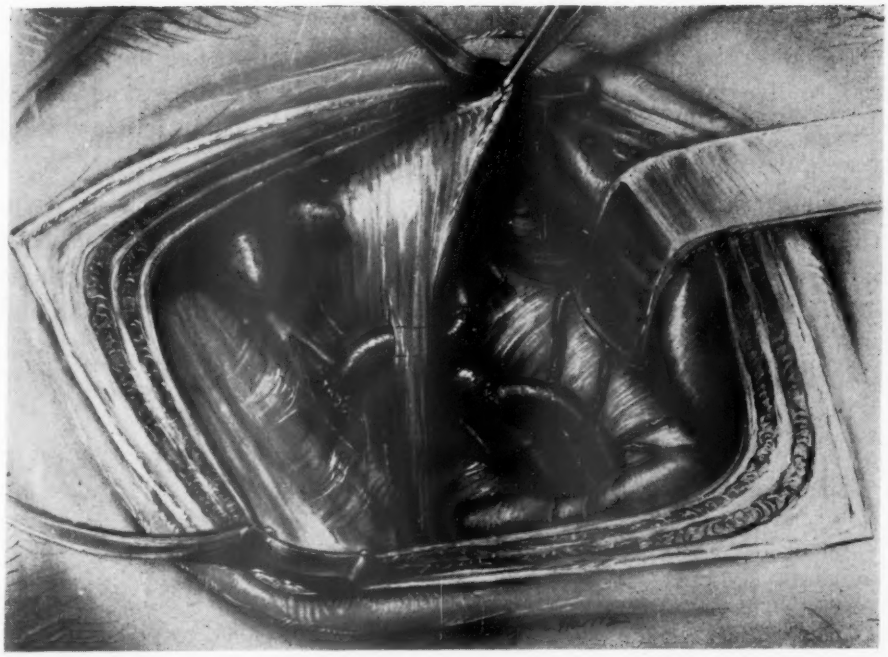

Fig. 1.—The completed operation, showing the graft from the aorta to the proximal stump of the portal vein and anastomosis of the distal portal vein to the side of the vena cava.

Fig. 2.—Aortic angiogram taken 6 weeks postoperatively, showing the irregular tubular vein graft going into the liver. The straight, smooth-walled arteries show well in comparison.

Fig. 3 is a drawing of the swollen, lobulated liver 8 weeks postoperatively.

Fig. 4 shows the rate of Bromsulphalein extraction in five operated dogs as compared to five normal controls. It is apparent that the extraction rate is faster in the operated animals. Five milligrams of bromsulfalein per kilogram of body weight were injected.

A catheter was passed through the jugular vein into the vena cava just above the entry of the hepatic veins. Blood samples were taken from this area and compared with samples taken from the femoral vein. Table I shows the results on 5 dogs which were operated upon as compared to 5 normal controls.

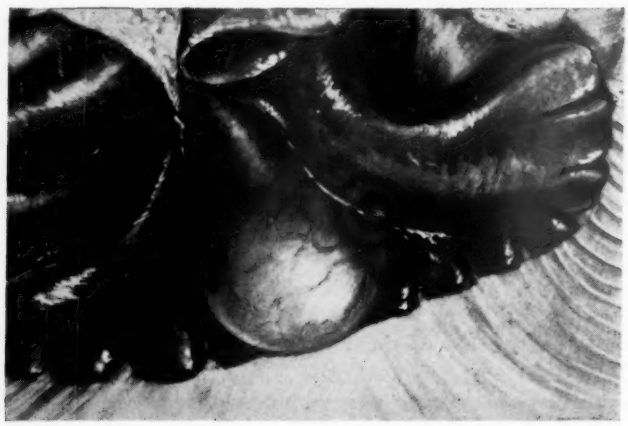

Fig. 3.—Lobulation and serration of the liver 8 weeks after operation.

It is apparent that there was no significant difference between the venous oxygen saturation of the dogs operated upon and the normal dogs.

Five dogs were examined 3 months postoperatively. The livers appeared swollen and red and the edges of all the lobes were serrated. In 2 animals the grafts were occluded nearly completely by fibrosis of the lumina. In 3 animals the grafts appeared patent. Microscopic examination of the liver showed that the cells were packed with glycogen granules (Fig. 5).

In 2 animals operated upon the hepatic artery was ligated at the hilum of the liver. Both animals survived the procedure without eventuality. Two weeks later the graft was ligated in both animals. Both died; 1 in 8 hours, 1 in 24 hours. It was apparent that in these 2 animals the graft was the sole blood supply to the liver.

TABLE I

	CONTROLS		OPERATED	
EXP. NO.	VENA CAVA O_2 SATURATION (PER CENT)	FEMORAL O_2 SATURATION (PER CENT)	VENA CAVA O_2 SATURATION (PER CENT)	FEMORAL O_2 SATURATION (PER CENT)
1	64	65	71	65
2	68	66	67	60
3	59	61	69	69
4	62	62	66	63

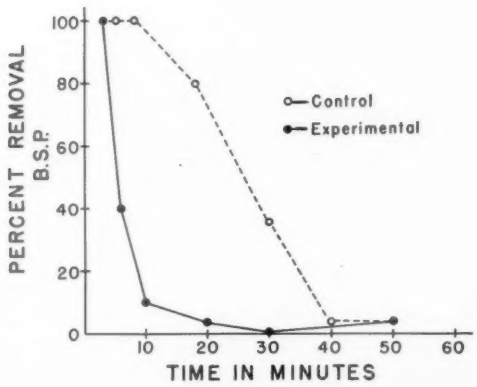

Fig. 4.—Graph showing the faster rate of bromsulfalein extraction in the animals operated upon, as compared to the controls.

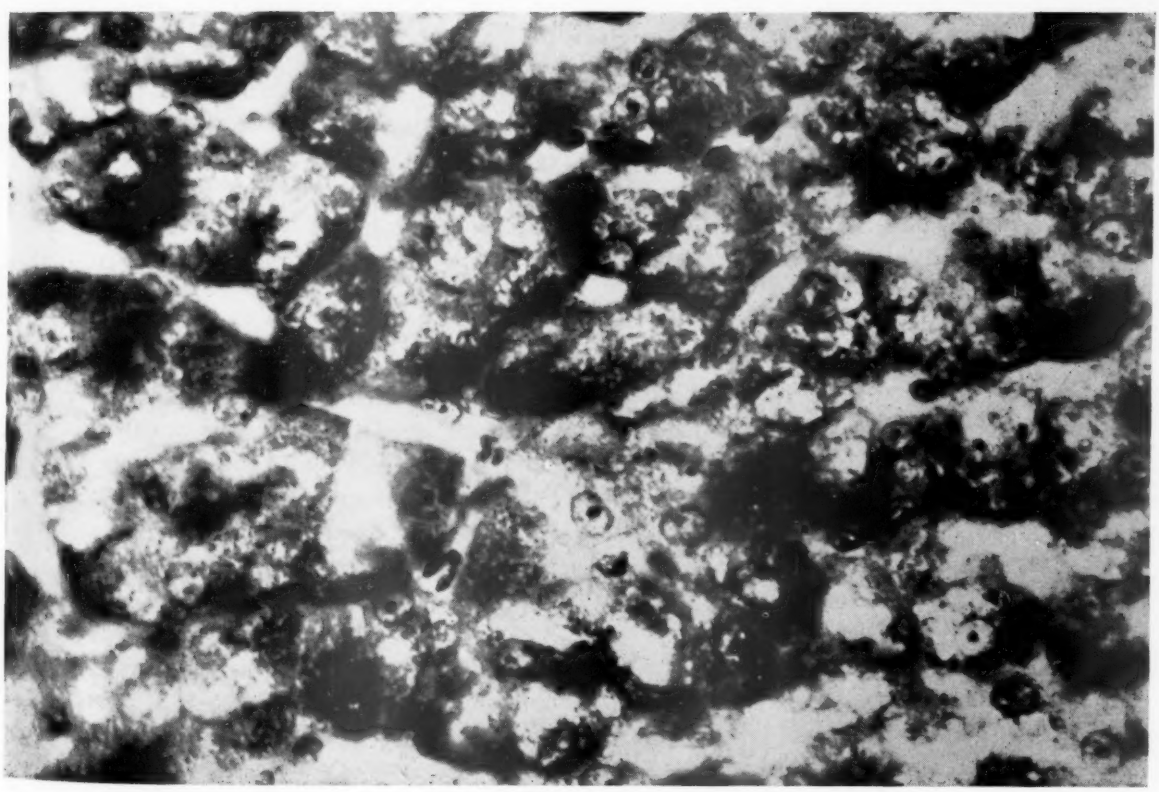

Fig. 5.—Glycogen stain of liver showing packing of cells with red-staining granules.

DISCUSSION

While it is not certain that portal hypertension is the direct cause of ascites and bleeding esophageal varices, there is enough clinical evidence to suggest that portal hypertension is certainly a factor in both these entities. However, the present operative procedures are all directed toward lowering the total blood flow to the liver. Even the suggested ligation of the hepatic artery, while theoretically increasing the venous flow through the liver, must lower the total flow, especially of blood at higher oxygen tension.

Since function of an organ is, in fact, dependent upon the blood flow, it follows that decreasing the blood flow will decrease function. The fact that no clinical effects are apparent in many cases is simply a measure of the natural reserve of the organ.

A procedure has been devised which increases the arterial blood supply to the liver while avoiding any increase of pressure in the portal venous system. No deleterious clinical effects have been noted in animals in whom arterialization has been present 1 year. The longest a graft has been proved open is 4 months.

The liver cells appear normal microscopically and function normally after this procedure, as far as ability to store glycogen is concerned. In fact, it is suggested that they are able to remove the additional oxygen brought to them by the arterial blood in the portal system.

While it has not been proved that the flow through the liver increases, studies of this aspect are now in progress.

SUMMARY

1. A method of arterializing completely the blood supply to the liver is described.

2. Under such circumstances, the liver of the normal dog appears to function efficiently.

THE TEMPORARY USE OF POLYETHYLENE SHUNTS IN THE RESECTION AND HOMOLOGOUS GRAFT REPLACEMENT OF THE AORTIC ARCH IN THE DOG

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IN A previous communication the temporary use of polyethylene shunts to make possible the resection and homologous graft replacement of certain major and vital blood vessels was demonstrated.[1] The temporary shunt, in this connection, acts much like the spontaneously developed collateral arterial circulation of patients with coarctation of the aorta. In the absence of such collaterals, with blood being diverted around the operative field through a plastic tube, one may cross-clamp the aorta and carry out deliberate dissection and suture, yet without danger of visceral and neurologic damage or cardiac failure.[7-10] Many methods for accomplishing this result have been described and the one which we have elected to use has been reported in detail.[1-6] The successful use of this method in resection and grafting of the abdominal aorta of man and of the descending thoracic aorta of dogs encouraged animal investigation of the problems concerned with its applicability to resection of the aortic arch. Our results may be conveniently considered under three subtitles: resection of the entire aortic arch, resection of the left half of the aortic arch, and aortic arch resection with continuous partial occlusion of the inferior vena cava.

GROUP I. RESECTION OF THE ENTIRE AORTIC ARCH

Eleven mongrel dogs were included in this group. Anesthesia was obtained by means of an ether-oxygen mixture administered endotracheally under positive pressure. Exposure of the aortic arch was made through an anterior transverse incision centered on the right third intercostal space and the bed of the resected left fourth rib. Procaine, 5 c.c. of a 1 per cent solution, was routinely injected into the pericardial sac. All pericardial, pleural, and fascial attachments were then severed from the aorta and its innominate branches from the aortic valve to the middle of the descending thoracic aorta. Adequate mobilization usually required ligation and division of 4 or 5 pairs of intercostal arteries. The proximal ends of three polyethylene shunts of appropriate caliber and length were then inserted into the anterior wall of the ascending aorta just distal to the aortic valve. The distal ends of these shunts were placed in the right and left innominate arteries and the mid-portion of the descending thoracic aorta, respectively. The ascending and descending aortas and the innominate arteries were then cross-clamped and the entire aortic arch and the origin of the innominate arteries resected. A frozen homologous aortic arch was then sutured

Read at the meeting of the Society of University Surgeons, Baltimore, Md., Feb. 7-9, 1952.

into the defect. Interrupted and continuous sutures of 00000 silk were employed. Clamps and shunts were then removed and the chest closed. Surviving animals were given penicillin and streptomycin postoperatively.

All but 2 of these 11 animals died either during operation or in the first 48 hours afterward (Table I). Death was usually due to cardiac embarrassment; though, in a few instances, uncontrollable hemorrhage was encountered. Two animals survived 10 and 42 days, respectively, 1 dying of pneumonia, and the other of causes that could not be determined. The average duration of aortic occlusion was 73 minutes. The average cross-sectional ratio of aorta to shunt was 9 to 1. Mediastinal and intrapericardial injection of procaine satisfactorily controlled cardiac arrhythmia, those animals dying of cardiac embarrassment usually showing a slowly progressive cardiac dilatation with ultimate failure.

GROUP II. RESECTION OF THE LEFT HALF OF THE AORTIC ARCH

In view of the prohibitive mortality encountered with this procedure a second group of 14 mongrel dogs was subjected to a less extensive operation. In these animals only the left half of the aortic arch and the left innominate artery were resected. Circulation through the right innominate artery was left intact and only a shunt between the ascending and mid-portion of the descending aortas was employed. The aorta was cross-clamped between its innominate branches and at the level of the last pair of divided intercostal arteries. After occlusion of the left innominate artery the left half of the arch was resected and replaced by a frozen homologous graft bearing the origin of the left innominate artery so that both aortic and innominate circulations were reestablished. Clamps and shunts were then removed and the chest closed.

All but 4 dogs died of cardiac failure either at operation or within the first 24 hours postoperatively (Table II). The four survivors lived 8, 12, 18, and 18 days and died of cardiac failure, wound dehiscence, pneumonia, and intractable diarrhea, respectively. The average duration of aortic occlusion was 39 minutes. The average cross-sectional ratio of aorta to shunt was 10 to 1. If one also considers the intact right innominate artery as a shunt the ratio becomes 4 to 1. Serial electrocardiograms were made at short intervals during and following operation on many of the animals in this and the preceding group. These showed ventricular strain patterns and bradycardia incident to procaine block and interruption of nerve fibers during dissection. Terminally ventricular tachycardia and fibrillation were often present.

GROUP III. AORTIC ARCH RESECTION WITH CONTINUOUS PARTIAL OCCLUSION OF THE INFERIOR VENA CAVA

In an effort to evaluate more precisely the effect of these operations on the heart, 4 dogs were prepared for continuous and simultaneous left ventricular blood pressure and electrocardiographic recording. Two animals were subjected to total arch resection and in the other two only the left side of the arch was removed. Before shunting or clamping, systolic ventricular pressure ranged from 90 to 120 mm. Hg (Fig. 1). After aortic cross-clamping and with the

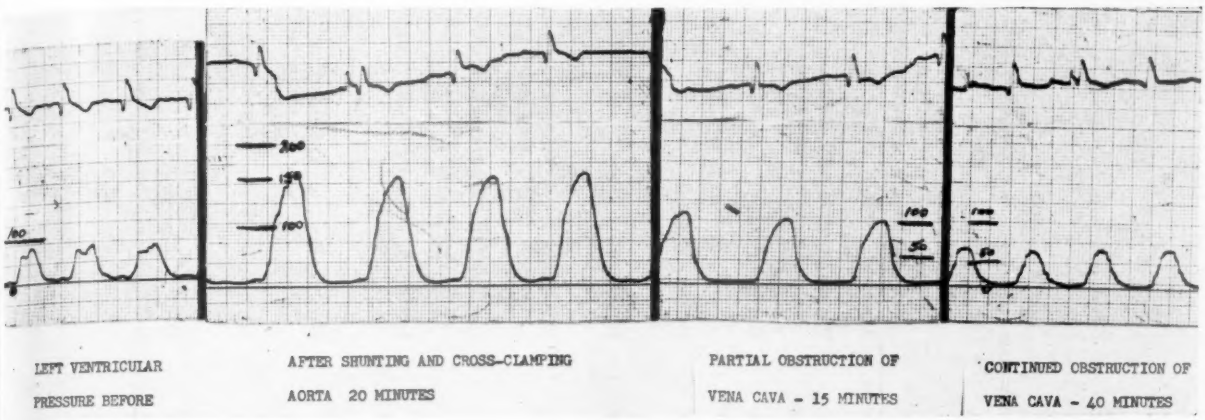
LEFT VENTRICULAR PRESSURE BEFORE
AFTER SHUNTING AND CROSS-CLAMPING AORTA 20 MINUTES
PARTIAL OBSTRUCTION OF VENA CAVA - 15 MINUTES
CONTINUED OBSTRUCTION OF VENA CAVA - 40 MINUTES

Fig. 1.—Effect of aortic occlusion and vena caval obstruction on left ventricular pressure.

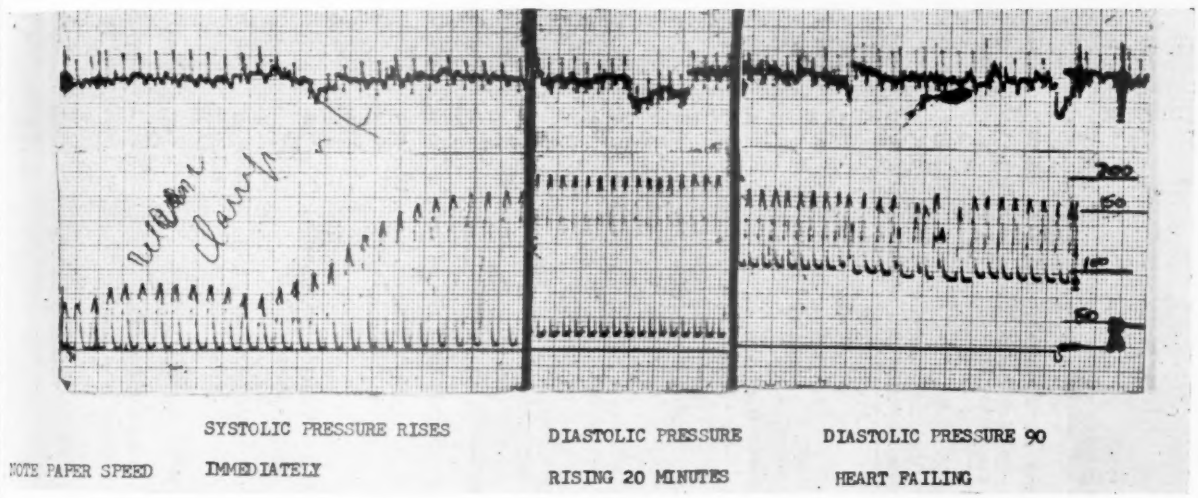
NOTE PAPER SPEED
SYSTOLIC PRESSURE RISES IMMEDIATELY
DIASTOLIC PRESSURE RISING 20 MINUTES
DIASTOLIC PRESSURE 90 HEART FAILING

Fig. 2.—Effect of releasing obstruction of vena cava on left ventricular pressure.

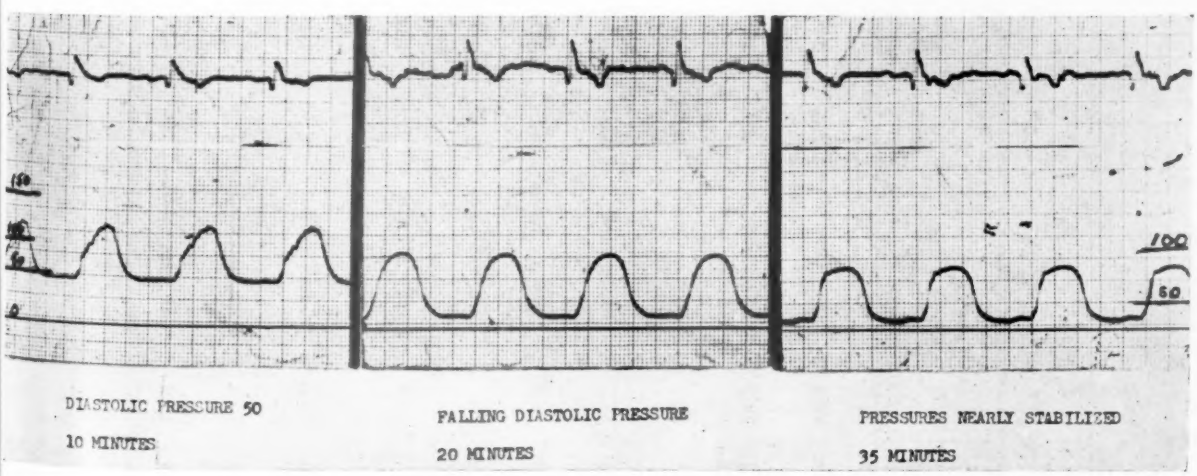

Fig. 3.—Effect of prolonged vena caval obstruction.

TABLE I. TOTAL AORTIC ARCH RESECTION

DOG NO.	WT. IN KG.	TIME AORTA CROSS-CLAMPED IN MIN.	INTERNAL DIAMETER IN MM.				CARDIAC COMPLICATIONS	LENGTH OF SURVIVAL	CAUSE OF DEATH	PROCAINE BLOCK OF MEDIASTINUM	OTHER MEDICATION
			AORTA	AORTIC SHUNT	INTERNAL CAROTID	TOTAL OF SHUNTS					
137	14.5	60	15	2.92	1.67	6.26	Arrhythmia, dilatation	16 hr.	Pulmonary edema, cardiac failure	Aborted arrhythmia	
30	13.9	90	11	2.69	1.67	6.03	Arrhythmia on cross-clamping	2 hr.	Cerebral anoxia, no spontaneous respiration	Lessened arrhythmia	Picrotoxin, metrazol
115	13.2	45	12	2.92	1.57	6.06	Hemorrhage on removing shunt—ascending aorta	Died on table	Shock—friable aortic wall	Predissection block	Transfusion
122	13.3	60	10	2.69	1.40	5.49	Slight dilatation at end of procedure	10 days	None apparent	Predissection block	
103	11.1	60	9	2.15	1.19	4.53	Arrhythmia during dissection, dilatation	2 days	Cardial failure, pulmonary edema	Lessened arrhythmia	
63	14.5	120	13	2.69	1.67	6.03	Ventricular fibrillation, dilatation of heart	Died on table	Cardiac failure	No block	Intracardiac procaine and adrenalin
40	11	55	10.5	2.15	1.19	4.53	Arrhythmia, dilatation	24 hr.	Cardiac failure	Lessened arrhythmia	Intracardiac procaine and adrenalin
50	13.5	60	12.5	2.69	1.67	6.03	Arrhythmia, slight dilatation	42 days	Pneumonia left lung, thrombosis left carotid anastomosis	Lessened arrhythmia	Oubain
20	12.7	45	10	2.15	1.19	4.53	Ventricular fibrillation	Died on table	Heart failure	No block	Intracardiac procaine and adrenalin
19	12.4	120	10.5	2.69	1.19	5.07	Ventricular fibrillation	Died on table	Heart failure	No block	Intracardiac procaine and adrenalin
114	11.2	90	9.5	2.15	1.19	4.53	Dilatation	Died on table	Heart failure	Block	

TABLE II. RESECTION OF LEFT CAROTID AND DESCENDING AORTA

DOG NO.	WT. IN KG.	TIME AORTA CROSS-CLAMPED IN MIN.	INTERNAL DIAMETER IN MM.		CARDIAC COMPLICATIONS	LENGTH OF SURVIVAL	CAUSE OF DEATH	PROCAINE BLOCK OF MEDIASTINUM	OTHER MEDICATIONS
			AORTA	AORTIC SHUNT					
79	12	60	10	2.69	Dilatation	12 days	Thrombosis of left carotid anastomosis, pleural-cutaneous fistula at sternum	Predissection	Oubain
102	13	30	11.5	2.92	Dilatation	8 days	Pulmonary edema, cardiac failure	Predissection	
38	12.6	45	11	2.92	Slight dilatation at end of procedure	18 days	Bilateral pneumonia	Predissection	
108	13	60	12.5	2.92	Moderate ventricular strain, hemorrhage on removing shunt	Died on table	Shock, friable aortic wall	Predissection	Transfusion
11	12		10	2.92	Standstill on insertion of shunt in ascending aorta	Died on table	Cardiac arrest	No block	
108	11	60	10	2.69	Progressive dilatation	Died on table on closing shunt	Cardiac failure	Predissection	Adrenalin
14	12.8	40	12	2.69	Hemorrhage—proximal shunt	Died on table	Shock	Predissection	Transfusion
115	11.2	50	9.5	2.69	None	1½ hr.	None apparent	Predissection	
46	13	45	12.5	2.92	Dilatation	Died on table	Cardiac failure	Predissection	Adrenalin
40A	13	60	12	2.92	Slight dilatation	24 hr.	Dissecting hematoma at site of shunt	Predissection	
106	13.5	30	11.5	2.69	Hemorrhage—proximal shunt	Died on table	Shock	Predissection	Transfusion
145	11.1	40	10	2.69	Dilatation	Died on table	Cardiac failure	Predissection	Adrenalin
134	11.4		9	2.69	Cardiac arrest on shunt insertion	Died on table	Standstill	None	Intracardiac procaine
128	13.5	30	9	2.15	Moderate dilatation	18 days	Severe diarrhea 16 days post-operatively	Predissection	

shunts functioning, systolic ventricular pressure rose promptly to 150 to 190 mm. Hg. Reducing cardiac inflow of blood by partial occlusion of the inferior vena cava slowly restored normal ventricular pressure. On releasing caval obstruction, systolic ventricular pressure rose precipitously to 170 mm. Hg and after 20 minutes had reached 200 mm. Hg (Fig. 2). By this time the diastolic pressure had begun to rise and the heart was noticeably overfilled with blood. Forty minutes after releasing caval obstruction, the systolic and diastolic pressures began to approximate each other at near 120 mm. Hg and the tensely distended heart neared failure. Even at this juncture partial inferior vena caval occlusion soon permitted the restoration of normal ventricular pressure and good heart action (Fig. 3). These observations closely paralleled those of Starling and associates in their study of the hemodynamics of a heart-lung preparation.[11-13] The 4 animals in this group had inferior vena caval occlusion throughout the period of aortic clamping, the degree of caval occlusion being varied to maintain normal left ventricular blood pressure and to prevent obvious cardiac dilatation. All survived operation and are alive at this time.

DISCUSSION

Cardiac deaths in these animals seem largely referable to the fact that the workload occasioned by aortic occlusion and the resistance of long rigid plastic tubes often exceed the physiologic limits of heart compensation. Cardiac denervation incident to the operation and deliberate procaine blocking to reduce arrhythmia abolish extrinsic reflex mechanisms which would increase cardiac efficiency by increasing rate. Cardiac dilatation and failure result as the expulsive force of the left heart becomes, beat by beat, progressively inadequate to overcome the increased resistance in its outflow tract. Trapping cardiac inflow of blood by partial occlusion of the inferior vena cava appears to be a satisfactory method of interrupting this vicious cycle.

CONCLUSION

By the temporary use of polyethylene shunts and partial occlusion of the inferior vena cava it appears possible to carry out resection and homologous graft replacement of the aortic arch of the dog.

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DISCUSSION

PROFESSOR RENÉ LERICHE discussed this paper in French.

Interpretation by Dr. Mark M. Ravitch: Professor Leriche said that a young French surgeon, Jean Oudot, had three patients with thrombosis at the termination of the common aorta whom he operated upon successfully. The first was a young woman who had a thrombosis of the terminal aorta and both iliacs. He had a human graft, cold preserved. Having had little experience at that time, he was able to make an anastomosis superiorly with the abdominal aorta and to one iliac, but the other side of the graft wasn't long enough and he was unable to make an anastomosis to the other iliac. After this first operation, he had a good pulsation on one side but not on the other. At the second stage, he performed an anastomosis from the successful graft of the iliac across to the other common femoral. That patient did perfectly well. The second and third cases, Oudot having had more experience, were perfectly simple. He performed a successful Y-anastomosis of both cases after resection of the common iliac and terminal aorta. Professor Leriche has examined all three of those patients and all three of them are well.

EARLY AND LATE EFFECTS OF VAGOTOMY ON GASTRIC SECRETIONS AND MOTILITY

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GENERAL interest in the physiologic effects of complete vagotomy developed with the early reports by Dragstedt and his associates[1-5] in 1943. In general, the extensive literature accumulating during the nine-year period is largely concerned with early effects on gastric secretions and motility and early efforts to evaluate the clinical utility of vagotomy alone or, usually and preferably, in combination with gastroenterostomy.

Our late clinical results in 175 patients treated during seven years and a comment concerning late insulin tests are described in a contemporary report.[6] The present study attempts evaluation of the early and late physiologic effects of vagotomy on those of the 175 patients whose gastric secretions have been determined and whose gastric motility has been studied using gastrometric methods. Certain reports of the early effects of vagotomy are reviewed to summarize present concepts.

Effect of vagotomy upon gastric secretions as reported by Dragstedt and associates[1-5] has, for the most part, been confirmed. Our first report[7] described reduction of volume and acidity of fasting gastric secretions, usually reduction or elimination of hypersecretion with insulin hypoglycemia and some reduction of the increase with histamine. It was evident that although pH increased and free and total acid decreased, the values for combined acid were greater after vagotomy. This indicated that the operation reduced the amount of acid secreted and facilitated neutralization. Occurrence of gastric retention or delay of emptying was demonstrated roentgenologically in those patients who had not had a previous gastroenterostomy or subtotal resection. It was also observed that the highest acidity of secretions of the fasting stomach and the greatest increase with histamine occurred among those patients with the greatest degree of retention or obstruction. Our later studies[8, 9] demonstrated that these effects on acidity and motility usually persisted at two and one-half to four years. Secretions with the caffeine tests were usually reduced. Failure of forceful thrust of the gastric content through the pylorus into the duodenum by failure of propulsive pyloric peristalsis was observed roentgenologically. Also these studies[7-9] reported results of gastrometric examinations employing balloons inflated to 300 c.c. and placed in the antrum and media. Vagotomy

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usually abolished or markedly reduced fluctuations of intragastric pressure of the fasting stomach, moderately increased resting tone, and eliminated the stretch reflex, but did not prevent occurrence of tonus contractions.

The latest report of Dragstedt and associates[10] indicates that nocturnal secretions were reduced from 74 to 11 meq. of free HCl in twenty-one patients tested at four years, and from 65 to 3 meq. in ten patients tested at five years, there being similar reductions in four patients tested at six years and one at seven. Of thirty-three patients tested using insulin hypoglycemia four years after operation, eleven had a "positive" response, three an "equivocal" response, and nineteen a "negative" response. Of fifteen at five years, eight were "positive," one "equivocal," and six "negative."* They found that the incidence of "positive" insulin tests is highest among those patients with the largest nocturnal secretions and that the incidence of recurrent duodenal or stomal ulcer, 6.6 per cent of their 516 patients, was most frequent among those whose secretions were high. Failure to secure healing of ulcer or recurrence was almost always associated with evidence of an incomplete vagotomy. Dragstedt and associates[11] have also studied the relative importance of the vagus, the antrum, and the intestine in animals. They find that 45 per cent of the gastric acid produced in a twenty-four hour period is caused by the nervous phase of secretion, about 45 per cent by the gastric or antral phase, and 10 per cent or less by the intestinal phase.

Moore and associates[12] described results in 116 patients followed five to forty-five months. Of these, ninety-one had transthoracic vagotomy without a drainage procedure. Laboratory status of all patients was not determined. Tests were reported in some, using small balloons placed in the pylorus to determine the motility pattern. Secretions of the fasting stomach and response to the insulin test were also studied in some of the patients. Moore concluded that decrease of motility and acidity is the typical postoperative picture in the resting unstimulated stomach following resection of the vagus nerves. These changes had for the most part disappeared by the end of one year. Continued abolition of secretory response to hypoglycemia, however, persisted in most patients. In a later report[13] Moore states that abolition of gastric secretory response to insulin-induced hypoglycemia is not a lasting result of vagotomy since it had been observed to re-establish itself two to four years afterward. He has since abandoned vagotomy and now favors subtotal gastric resection.

Machella and Lorber,[14] using their method of balloon-kymographic recording and studying twenty-four patients, observed absence of antral peristalsis or diminished peristalsis. Peristalsis returned following Urecholine, an observation which we confirmed.[8]*

Walters and Fahey,[15] in 1950, described results in forty-two of their sixty-eight patients who had been re-examined. They state that 80.9 per cent lost gastric tone and motility two and one-half weeks after operation, but that at ten months 70.3 per cent had regained normal gastric tone and at eighteen months, 79.4 per cent. These observations were based upon indirect estimation

*The currently employed dose of Urecholine is 2.5 mg. subcutaneously or 20 to 30 mg. orally.

during roentgenologic observation rather than direct gastrometric measurement. He states that in the immediate postoperative period free hydrochloric acid determined during an Ewald test meal was reduced, or there occurred relative achlorhydria in 69.1 per cent, there being no reduction of free acid in 19 per cent. In the remaining 11.9 per cent the amount of reduction, if any, was unknown. Eighteen months after operation free acid was reduced or relative achlorhydria deveolped in 78.6 per cent, there being no reduction of free acid in 9.5 per cent of the cases; the amount of reduction, if any, was unknown in 11.9 per cent. The insulin test gave negative results in 85.7 per cent immediately after vagotomy and in 78.6 per cent at eighteen months. In a later study of 141 cases Walters and Belding[16] reported tests in eighty-five patients one to four years after operation. Of twenty-two with vagotomy and no drainage procedure, reduction of acidity was found in 50 per cent, achlorhydria in 20.3 per cent and no reduction or return to preoperative levels in 23.7 per cent. However, when simultaneous or previously performed gastroenterostomy, pyloroplasty, or gastric resection was associated with vagotomy, reduction of gastric acidity to achlorhydric levels occurred in a greater number of cases and was even more apparent in the late postoperative period. There was a return to preoperative levels in only 7 per cent of the group. Motility determined by roentgenologic methods at one to four years after operation was absent or decreased in 26.4 per cent of the patients with vagotomy the only procedure performed, and 3.6 per cent of the patients who had associated drainage procedures. Walters questions the significance of the insulin test since, in four patients of seven treated by section of the posterior vagus nerve without cutting the anterior vagus, a negative insulin test occurred.

Stein and Meyer[17] reported results of carefully performed studies in twenty-one of their patients tested three to four years after vagus section. Effects of the insulin test on acidity and motility were obtained simultaneously by passing a Levin tube well into the stomach for suction and another Levin tube with a balloon attached into the cardiac end of the stomach. The balloon was inflated by 10 to 15 c.c. of air. Observations continued an hour before and up to two and one-half hours after insulin. Four of the twenty-one patients were considered as having "normal vagus function." Their average greatest acidity occurred one hour and fifteen minutes after insulin and reached 7 meq. of HCl. Ten patients were considered as having "partial vagus function." Their average greatest acidity occurred one hour and thirty minutes after insulin, reaching 1 meq. of HCl. Seven patients were considered as having "no secretory response and no vagus function," since no free acid was produced during the two and one-half hours after insulin hypoglycemia. Tracings of changes of pressure within balloons revealed that each of the four patients with "normal vagus function" had typical gastric hunger contractions, similar to those present in all patients before vagus section. The ten patients with "partial vagus function" had irregular low gastric contractions. The seven with "no vagus function" had occasional tonus rhythm but no hunger contractions. Basal secretions were determined, using the fifteen-minute specimens obtained before the period of testing. There were no secretions in the

seven patients, moderate secretions in nine, and normal secretions in four. Acidity with the histamine test was reduced or low in all patients except the four with "normal vagus function." Acidity with the caffeine test was similarly reduced. Using different techniques these authors have confirmed our observations.[7-9]

The references above summarize only part of the literature. They are, however, presented as typical examples of results of study. It is evident that differences of opinion exist as to the incidence of significant changes of gastric secretion and motility following vagotomy, and the number of years such changes as were effected persisted. Differences of methods of examination may explain some of the discrepancies. Acidity of fasting secretions in several reports has been determined using twelve-hour nocturnal aspirations, Ewald test meals, or control aspirations preparatory to other tests. Motility has been determined by roentgenologic examination only or by gastrometric methods using small balloons in the pylorus, small balloons in the antrum, or 300 c.c. balloons in the antrum and media of the stomach.

Techniques for determination of secretions during insulin hypoglycemia have also varied. Hollander[18] emphasized details of his original technique and stated that the insulin test must be considered in relation to all gastric secretory nerves, and not restricted to presence or absence of the gastric vagi alone. He stated that the symptoms of hypoglycemia afford poor correlation between their time of onset in different subjects and the degree of hypoglycemia; determination of blood sugars was considered necessary at the end of the first half hour and at a second or even a third half hour. He stated that if there was no significant rise in the free acidity curve and the blood sugar fails to reach 50 mg. the test must be declared invalid. A positive response was indicated by a well-defined rise in the free acidity curve following injection, that is, two or more successive points on the curve must lie distinctly above the base line established by the resting specimens. At least one of these points should be elevated by 20 mN or more above the control values, unless these resting specimens contain no free acid in which case he considered a 10 mN rise significant. A true negative reaction requires that the patient must be capable of secreting hydrochloric acid as shown by a previous histamine or other test and the acidity curve must either be flat or show a downward slope without a subsequent rise. He stated, however, that acidity sometimes fluctuates above and below the control value, especially in postvagotomy patients. He further stated that if the resulting acidity curve does not clearly conform to the criteria for either a positive or a negative response, such a test was declared equivocal. He emphasized that the height of the acidity curve above the control level, the duration of the elevated portion and the latent period between the time of injection and beginning of the rise of acidity varied extensively. He stated, therefore, that the test cannot serve as a quantitative indicator of the degree of innervation remaining after a partial vagotomy. The need for repeated postoperative insulin tests is stressed.

The report by Weinstein, Hollander, Lauber, and Colp of results of the insulin tests in 125 patients with vagotomy is, therefore, important.[19] Of

twenty patients with vagotomy alone for uncomplicated ulcer the test was considered negative in twelve and positive in eight. Of twenty-eight patients with vagotomy and gastroenterostomy for duodenal ulcer the test was considered negative in eleven, positive in twelve, and equivocal in one, here being no free acid in four patients. Of fifty-eight with vagotomy and subtotal gastrectomy the test was considered negative in twelve, positive in ten, and equivocal in two, there being no acid in thirty-seven. Where vagotomy was performed for gastrojejunal ulcer in nineteen patients, the test was negative in one, positive in nine, equivocal in one, and there was no free acid in eight. Thus positive postoperative tests according to Hollander's criteria were obtained in 29 per cent of all patients tested after vagotomy.

We respect the criteria which Hollander has arbitrarily established but since the latent period between the time of injection of insulin and the beginning of a rise of acidity frequently seemed prolonged after vagotomy[7] our collections of gastric content have continued at half-hour intervals for five hours following the insulin rather than only two hours. Because of the practical difficulties incident to repeated determinations of blood sugar and because of the wide variation of responses of acidity often in the same patient from time to time, few investigators, ourselves included, have employed the exact method and interpretation of Hollander. Our blood sugars, for example, are determined only once, forty-five minutes after the insulin and specimens of gastric content are obtained each half-hour for five hours. Variations of results of the insulin test as described above may relate to the various techniques and interpretations.

Because of the variations of observations in the reports on motility and acidity referred to above we have reviewed all secretory and gastrometric studies obtained in the 175 patients[6] treated by vagotomy (June 1944 through May 1951) to determine how late results obtained by our methods, previously described,[7-9] compare with those of other investigators and to learn how many of these patients had high secretions and strong motility during the first months and several years after operation.

There was one operative death among the 175 patients. Of fifty patients originally treated by vagotomy alone for duodenal ulcer thirty remain without secondary operation. One hundred twenty patients had vagotomy and some form of gastroenterostomy, including those treated primarily by vagotomy and gastrojejunostomy, or receiving a secondary drainage operation, or treated by vagotomy for jejunal or stomal ulcer following previous gastroenterostomy. Fifteen patients had vagotomy and a subtotal gastric resection, including thirteen treated by vagotomy for stomal ulcer following resection and two treated by resection following vagotomy without drainage. Nine patients were treated for gastric ulcer. Results will be listed according to these four groups.

METHOD AND CONTROL OBSERVATIONS

Duodenal Ulcer Patients

Previous reports[7-9] based results upon comparison of pre- and postoperative examinations. Results described in this report will also refer to pre- and post-

operative examinations whenever these were obtained. Postoperative examinations only have been obtained in many of the 175 patients and no examinations were made in a few. Therefore, to further aid evaluation by establishing reference or control values for comparison, control observations in patients who had duodenal ulcer and no operation as well as preoperative observations in patients who later had operation have been collected.

Gastrometric Studies.—Total resting intragastric pressure and fluctuations of total intragastric pressure were measured by introducing a rubber balloon into the stomach, connecting it to a recording bromoform manometer and inflating it at two- or three-minute intervals with successive 50 c.c. increments of air to a volume of 300 c.c. Recordings were continued forty-five minutes to three hours. The latex balloons employed measured 8 to 10 cm. in length and 3 to 4 cm. in diameter when inflated. Their position within the stomach has been determined by use of the fluoroscope in many patients. The proximal part of the balloon located itself in the cardia and the distal end in the midstomach or proximal pylorus. The balloon attached to a Levin tube was introduced after a twelve-hour period of fasting. Before or after introduction into the stomach the balloon was inflated to a volume of 300 c.c. to record its intrinsic pressure by the bromoform manometer. After introduction into the stomach the balloon was inflated by 50 c.c. increments of air to observe occurrence of stretch reflexes. Thereafter the patient, the balloon, the manometer, and the long-paper-recording kymograph were left undisturbed for forty-five minutes or longer. Fluctuations of total intragastric pressure and tonus contractions, should these occur, were observed and recorded. In some patients intramuscular injections of caffeine and sodium benzoate, 0.5 Gm., or of Banthine, 100 mg., were then administered again leaving the patient and recording system undisturbed another hour or longer.

The pressures necessary to inflate the balloons to a volume of 300 c.c. before or after they were placed in the stomach varied from 1.5 to 2.1 cm. of bromoform, 4.0 to 5.8 cm. of water.*

Total resting intragastric pressure is defined as the combined intra-abdominal and intragastric pressure after subtracting the intrinsic pressure of the balloon.† Total resting intragastric pressure, commonly referred to as intragastric tone, was calculated during intervals between contractions by doubling the height of the manometer tracings above the base line of the recording system and subtracting the intrinsic pressure of the balloon. Most of this measured pressure is caused by partial contractions of the smooth muscle of the gastric wall on the stomach content. Fluctuations of total intragastric pressure are defined as waves of gastric contractions causing changes of pressure above or below this level.† This was also calculated by doubling the height of the excursion of the manometer tracing.

*In previous reports pressures recorded by the bromoform manometer were converted into equivalent values for water. In this paper values will be presented in terms of centimeters of bromoform since bromoform manometers which fluctuate less widely than water manometers are more satisfactory for gastrometric studies and are frequently used.

†As reported[3] in terms of centimeters of water for thirty patients tested before vagotomy, the average resting pressure was 4.0. For forty-two tested during the first two weeks afterward the average was 8.2 cm. and for eleven at one to two and one-half years it was 10.5 cm. Amplitude of gastric contraction waves averaged 20.5 cm. of water before vagotomy, 0.6 cm. soon afterward and 2.8 cm. at one to two and one-half years.

Values for resting intragastric pressure, or tone, and for fluctuations of intragastric pressure, or contractions, will be presented as the average of the pressures of all patients tested during each time period before and at intervals after vagotomy. The average of the resting intragastric pressures determined in eighty-six patients with duodenal ulcer and without operation was 2.2 cm. of bromoform. The range was 5.4 cm. to 0.4 cm. of bromoform. The average fluctuations of intragastric pressure above this level for these control patients was 2.2 cm. The range was 7.6 to 0.2 cm. Many of the patients exhibited stretch reflexes during the inflation of the balloons with 50 c.c. increments of air at the start of each test and a few exhibited tonus contractions during the course of the forty-five-minute to three-hour observation continued at the 300 c.c. volume.

Insulin Tests.—After a twelve-hour period of fasting a Levin tube was introduced into the stomach and residual gastric content aspirated and discarded. The Levin tube was then clamped between aspirations which were made at half-hour intervals, one or two before, and ten after, administration of insulin. Regular insulin was then given intravenously immediately after the last control aspiration using 20 units for most patients and 15 units for the few who were slight or were markedly undernourished. It is recognized that some secretions might have been lost through the duodenum during each half-hour period. However, the insulin test is based upon increase of free acid without regard to volume of secretions.

Values for free acid of the control half-hour collections of twenty-four patients with duodenal ulcer and no operation averaged 43.4 and ranged from 111 to 0.* Blood sugar was determined for each patient forty-five minutes after the injection of insulin. The average blood sugar was 56 and the range 85 to 37 mg. per 100 ml. We cannot exclude nineteen tests in which the blood sugar was somewhat higher than 50 mg. since determinations at more frequent intervals might have demonstrated lower levels. Increase of free acid occurring in these nineteen patients equaled that occurring in the others.

The insulin test has been interpreted and reported according to the highest value for free acid or the highest two values for free acid; the latter interpretation is preferred by Hollander.[18, 19] As the individual curves representing increases in our patients were studied, it became evident that single aberrant high readings occasionally occur. Interpretation in terms of the average of the highest and the next highest reading in each patient most accurately represented the individual curves. Accordingly the two highest readings for each patient will be considered in this presentation.

It is of interest to consider the time of occurrence of the maximum amounts of free acid so that results of our tests may be related to results of others using a two-hour collection period. The two highest readings in the five-hour period for these twenty-four control ulcer patients occurred during the first two hours in nine and during the next three hours in four. In the remaining eleven patients one of the two highest readings occurred in the two-hour period and the

*Reference to values for free acid hereafter will refer to milliliters of N/10 hydrochloric acid per 100 ml. of gastric juice. This value is that commonly referred to as a clinical unit.

other in the subsequent three-hour period. The average of the values of the forty-eight highest readings for free acid in the twenty-four patients was 94 and the range 133 to 58. An increase above control values for free acid of more than 20 occurred in each patient during the two- and the three-hour periods.

Fasting Secretions.—Continuous twelve-hour overnight aspirations of gastric secretions were started at 8 or 9 P.M. using a No. 14 F Levin tube and discarding residual juices. The patients were allowed liquid feedings at 6 P.M. Continuous suction was accomplished using a water gravity system and gastric secretions were collected in a trap bottle capable of handling volumes up to 4,000 c.c. Collections continued through the night to 8 or 9 A.M. This method closely resembles that used by Levin, Kirsner, Palmer and Butler in normal individuals[20] and in patients with duodenal ulcer.[21] Since we have no observations on normal individuals and can make no comparison between normal and ulcer patients their figures are quoted for reference. Their average volume for fifty studies in twenty-one normal males and twelve normal females was 581 c.c., the range being 1,188 to 173 c.c. The average free acidity was 29 clinical units, range 90 to 1. Their average volume for thirty-two patients with duodenal ulcer was 1,004 c.c., range 1,389 to 362 c.c. The average free acidity was 61 clinical units, range 112 to 13. Our average volume for seventy-five patients with duodenal ulcer and without surgery was 784 c.c., range 3,300 to 68 c.c. The average of values for free acid was 41, range 83 to 0. We have not been able to determine validity of minimum determinations of volume or of free acid. It is possible that the Levin tube used for suction occasionally passed through the pylorus into the duodenum during the night hours, thus giving occasional partial collections and facilitating neutralization of acid. For example, eight volumes among the seventy-five patients were below 200 c.c., the lowest 68 c.c. These low readings are included in the average since the same error or questionable low volumes were also included in patients aspirated after vagotomy and since there was no valid reason for discarding any reading, however improbable. Six of the seventy-five patients had low values for free acid 0, 0, 5, 7, 9, and 10.

RESULTS OF VAGOTOMY FOR DUODENAL ULCER

Fifty patients were treated by transthoracic vagotomy for duodenal ulcer without using any drainage procedure. Thirty of these patients have had no secondary operation, eighteen, at some time during their postoperative course, had secondary gastroenterostomy, and two had secondary gastric resection. Results of those of the thirty tested following vagotomy alone and those of the nineteen tested between vagotomy and their secondary operation will be presented in this section. Results after secondary operation are entered in the later sections: vagotomy with gastroenterostomy and vagotomy with subtotal gastric resection.

Gastrometric Studies.—Altogether thirty-one of the fifty patients treated by transthoracic vagotomy for duodenal ulcer have had gastrometric studies. Of these, twenty-one had preoperative and postoperative tests. Their preoperative resting intragastric pressure or tone averaged 1.8 cm. of bromoform, range

3.4 to 0.4 cm. Average of fluctuations of intragastric pressure was 4.4 cm., range 10 to 0.8 cm. Their postoperative studies, early and late, numbered forty-four. Considering all postoperative tests at different times, the average resting intragastric pressure, or tone, was 3.2 cm., range 7.0 to 1.2 cm. The average of fluctuations of intragastric pressure, or contractions, above this level in twenty patients was 0.3 cm., range 1.4 to 0 cm. One of the twenty-one patients, J. C., had similarly increased tone and reduced contractions ten days after vagotomy but five months later exhibited frequent but regular contraction waves representing pressure fluctuations of 3.4 cm. An insulin test at this time produced maximum values for free acid of 28 and 36. Eleven patients were tested only after vagotomy and their twenty-seven tests, early and late, had an average resting intragastric pressure of 3.0 cm., range 4.4 to 0.6 cm. Their fluctuation pressures averaged 0.4 cm., range 1.6 to 0 cm.

Of the thirty-one patients tested postoperatively, twenty-six were studied during the first three weeks. Their average tone was 2.8 cm., range 6.0 to 0.6 cm. The average of contraction pressures was 0.2 cm., range 1.2 to 0 cm. Nineteen patients were tested three months to one year after operation. Their average tone was 3.4 cm., range 5.2 to 2.0 cm., and their average of fluctuations was 0.4 cm., range 1.4 to 0 cm. The pressures of patient J. C. are not included in this average and range. Eleven patients were tested one year to six years and ten months after vagotomy, average three years and two months. When patients had more than one gastrometric study only the latest is now considered. Average tone was 3.6 cm., range 7.0 to 0.8 cm. Average of contraction pressures was 0.4 cm., range 0.8 to 0 cm.

Examination of sequences of tests for individual patients reveals the slight increase of resting intragastric pressure indicated by the average figures. There was no tendency for return of forceful contractions. Stretch reflexes did not occur in any patient following vagotomy but tonus contractions occurred occasionally.

Insulin Tests.—Of fifteen patients tested during the first thirty days following transthoracic vagotomy, nine had no free acid during the two hours following insulin. Of these, there was no free acid during the next three hours in seven, values for two patients increasing in at least two specimens, one less than 20 ml. N/10 HCl per 100 c.c. of gastric juice and one more than 20 but not to control insulin test levels. Six patients had moderate amounts of free acid which did not change or increased less than 20 in the highest two specimens during the first two hours, there being no further change in the next three hours.

Eleven patients were tested at three months to one year, average five months. Of these, three had no free acid in any specimen. Seven had values less than 20 in the highest two specimens during the first two hours. Of these, during the next three hours one had no free acid, one increased to more than 20 but did not reach values of the control tests. Two increased to values of 65 and 70 (patient E. H.) and 65 and 65 (patient C. W.). These values reached the range of control ulcer patients for two specimens only in the last three hours of the five-hour test.

Eighteen patients were tested at one to six years, average three years and one month. When patients had more than one insulin test only the latest is now described. Five had no free acid during the first two hours following insulin and of these there was no free acid during the next three hours in two; three developed values for free acid of less than 20. Eleven patients had moderate amounts of free acid which did not change or increased less than 20 for the highest two values during two hours. Of these, three increased more than 20 during the next three hours, two decreased to no free acid and the remainder continued as during the first two hours. Two patients developed values for free acid of more than 20 in the highest two specimens but did not reach the levels of control patients during the first two hours or during the next three. One of the eighteen patients described above as having moderate amounts of free acid or increasing less than 20 during the two-hour period and then increasing more than 20 for two readings in the next three hours (patient G. F.) nevertheless had single readings in each period equaling values of control insulin tests and on the basis of the five-hour period should be considered as having his two highest readings equal to those of the control group.

Of the eighteen patients tested at one to six years, eight had an earlier test in this time period. The earlier test produced somewhat lower amounts of free acid in three patients, equal amounts in three, and higher in two. One of the two patients (L. H.) had two values, 64 and 66, in the first two hours of a test at one year, and during the test at four years and three months had increases not exceeding 20 during the entire five-hour period. The other patient (D. P.) during a test at three years had values in the three-hour period equal to those of control patients, 64 and 71, but during the test at five years had no increase during the entire five-hour period.

It is of interest that blood sugars obtained forty-five minutes after insulin in these patients after vagotomy alone averaged 47 mg. per 100 ml., range 85 to 30. These values are slightly lower than those obtained in the twenty-four patients with duodenal ulcer described under Method and Control Observations.

Fasting Secretions.—Altogether thirty-seven of the fifty patients treated by transthoracic vagotomy for duodenal ulcer have had determinations of volume and acidity of twelve-hour overnight collections of gastric content. Of these, thirty-one had preoperative and postoperative determinations. Their preoperative volumes averaged 841 c.c. and ranged from 2,200 to 105 c.c. Their postoperative determinations, early and late, numbered seventy-three. Considering together all specimens at different times the average postoperative volume was 319 c.c., range 1,200 to 13 c.c. Six patients were aspirated only after vagotomy and their eleven tests averaged 185 c.c., range 495 to 25 c.c.

Of the thirty-seven patients tested postoperatively, C. W. is considered a definite hypersecreter. Volumes were 1,830 c.c. before vagotomy and consecutively 500, 1,200, and 450 c.c. during two years afterward. His insulin tests eight months after vagotomy produced values during the three-hour period of 65 and 65. On two subsequent occasions, at seventeen and eighteen months, tests produced values of 49 and 50 and of 50 and 50. Gastroenterostomy was

then done and two years later the twelve-hour volume was 285 c.c. and the highest two readings during five hours after insulin were 28 and 38. Another patient (W. D.) had volumes of 800 c.c. nine days after vagotomy and 888 c.c. two years later. Corresponding insulin tests produced high readings of 39 and 40 and of 41 and 56, each occurring during the three-hour period. However, since there was no free acid in either of the overnight suctions this patient is not considered a hypersecreter. Thirteen patients included in the averages above had occasional volumes of over 500 c.c. Two patients had volumes of 775 and 800 c.c., respectively, but their overnight suctions were obtained three and four days after surgery and additional tests have not been made. There was no free acid in either of these specimens. The remaining eleven patients each had repeated tests and in one of these for each patient volumes were as large as 500 to 650 c.c., while in the other tests for each patient volumes were lower.

Volumes of overnight collections of gastric content have been measured at two to six years, average three, in fifteen of the thirty-seven patients tested after vagotomy. The average volume of the latest test in the fifteen patients was 248 c.c., range 888 to 13 c.c. This average and range are lower than that of all postoperative readings early and late in the thirty-seven patients. Also examination of the sequence of tests for each of the thirty-seven patients revealed no increase of volume in the latest readings. Therefore, these observations following transthoracic vagotomy for duodenal ulcer do not produce any evidence that volumes are any higher after several years than volumes obtained during the first months or years.

Values for free acid, milliliters N/10 HCl per 100 ml. of gastric juice have been ascertained in the twelve-hour collections of the thirty-one patients having pre- and postoperative tests. Twenty patients had no free acid in any of forty-three determinations made early and late after vagotomy. Their values for free acid averaged 44 and ranged from 83 to 6 before vagotomy. Eleven patients had free acid in most of thirty determinations made early and late after vagotomy. Their values for free acid averaged 51, range 71 to 25, before vagotomy and averaged 19, range 55 to 0, after vagotomy. Acidities of 55 occurred in two of these patients. Insulin tests produced a high value for free acid of 36 at the end of two hours in one and a high of 50 at the end of four hours in the other. Six patients were tested using overnight suctions only after vagotomy. Five had no free acid and one had 32 units.

Of the thirty-seven patients tested following transthoracic vagotomy observations have been obtained in fifteen at two to six years, average three. Nine had no free acdi. Some free acid was present in six, values averaged 28, range 37 to 12. Examination of the individual sequences for each patient revealed some increase of acidity in the later readings in two, no change of acidity in one, reduction in the later readings in three, and no free acid in any reading in nine.

VAGOTOMY AND GASTROENTEROSTOMY FOR DUODENAL AND JEJUNAL ULCER

Eighty-eight patients were treated primarily by vagotomy and gastroenterostomy for duodenal ulcer. Fifteen had jejunal ulcer following previous

gastroenterostomy. Vagotomy and gastroenterostomy also existed in seventeen patients treated for duodenal ulcer by transthoracic vagotomy and subsequently requiring a drainage procedure. These three groups of patients, total 120, are considered together, giving results in those tested, dating tests as following vagotomy, and including no observations preceding secondary gastroenterostomy in the seventeen patients.

Gastrometric Studies.—Altogether thirty-four of the 120 patients have had gastrometric studies. Of these seventeen had preoperative and postoperative tests. Their preoperative resting intragastric pressure or tone averaged 2.4 cm. of bromoform, range 5.4 to 0.2 cm. Average of fluctuations of intragastric pressure was 4.8 cm., range 7.6 to 2.6 cm. Their postoperative studies, early and late, numbered thirty. Considering all postoperative tests, early and late, together the average resting intragastric pressure, or tone, was 3.4 cm., range 5.4 to 1.2 cm. The average of fluctuations of intragastric pressure, or contractions, was 0.4 cm., range 1.8 to 0.0 cm. Seventeen patients were tested only after vagotomy. Of these, fourteen evidenced typical increase of tone and marked decrease of fluctuations. The average resting intragastric pressure for the fourteen, early and late, after vagotomy was 3.4 cm., range 6.6 to 1.2 cm. Average of fluctuations of intragastric pressure was 0.3 cm., range 1.8 to 0.0 cm. Three of the seventeen patients tested only after vagotomy exhibited marked fluctuations of intragastric pressure, or contractions. Resting intragastric pressure was 6.6 cm. for one (J. F.), 2.0 cm. for one (T. W.), and 4.4 cm. for the third (S. S.). Fluctuations of intragastric pressure were 2.2 cm. for J. F., 3.6 cm. for T. W., and 3.4 cm. for S. S. As described in the next paragraph presenting the insulin tests, two of these patients (J. F. and S. S.) developed two highest values for free acid equal to those for patients of the control ulcer group and one (T. W.) developed one value for free acid within the control range. Each of these three patients has had recurrence of ulcer. Of the thirty-three patients tested postoperatively fourteen were studied during the first three weeks. Their average tone was 2.6 cm., range 4.2 to 0.3 cm. The average of the fluctuations of intragastric pressure was 0.2 cm., range 1.0 to 0.0 cm. Fourteen patients were tested three months to one year after operation. Their average tone was 2.8 cm., range 6.0 to 1.4 cm., and their average of fluctuations was 0.4 cm., range 1.0 to 0.0 cm. Fifteen patients were tested one year to six years and two months after vagotomy, average three years. When patients had more than one gastrometric study only the latest is now described. Average tone was 4.0 cm., range 5.4 to 2.4 cm. Average of fluctuations was 0.6 cm., range 1.8 to 0.0 cm.

Examination of sequences of tests for individual patients reveals the slight increase of resting intragastric pressure indicated by the average figures. There was no tendency toward return of forceful contractions except in the three patients previously mentioned as having recurrence of ulcer. Stretch reflexes did not occur in any patient following vagotomy but tonus contractions occurred occasionally.

Insulin Tests.—Altogether eighty-seven of the 120 patients with vagotomy and gastroenterostomy have had insulin tests. Forty of these patients were

tested during the first three weeks. In twenty there was no free acid during the first two hours following insulin. Of these, there was no free acid during the next three hours in fourteen, four increased less than 20 ml. N/10 HCl per 100 ml. of gastric juice in at least two specimens, and two increased more than 20 but not to control insulin test levels. Fifteen patients had moderate amounts of acid which did not change or increase less than 20 in the highest two specimens during the first two hours. Of these, there was no further change in the next three hours in ten and there was an increase of more than 20 but not to control test values in five. Four patients increased more than 20 during the first two hours and of these there was no further change in two, and acidity in two decreased. One patient (F. S.) developed values of 65 and 85 during the first two hours and also values of 87 and 106 during the second three hours, these values equaling those of control tests.

Of fifty-seven patients tested three months to one year, average five months, after vagotomy there was no free acid during the first two hours in thirty-five. Of these, there was no free acid during the next three hours in twenty-four, eight increased less than 20, and three increased more than 20 but not to values equal to control tests. Nineteen patients had increases of less than 20 during the first two hours. Of these, the values for ten remained the same during the next three hours and values for one decreased; values for eight increased more than 20 in three and equal to control tests in five, 71 and 83 for patient F. S., 61 and 65 for patient J. C., 62 and 71 for patient B. D., 74 and 64 for patient J. F., and 66 and 70 for patient I. S. Two patients (S. S. and T. W.) had increases of more than 20 during the first two hours and also during the three hours. One reading only during the three hours equaled values of control tests. One patient (C. M.) had two readings, 66 and 71 during the first two hours, equal to control tests, and had lower readings, increases of less than 20 during the next three hours.

Forty-seven patients were tested one year to six years and eight months, average three years, after vagotomy. When patients had more than one insulin test in this period the latest test is described. Twenty-two had no free acid during the first two hours following insulin and of these there was no free acid during the next three hours in seventeen, five increasing less than 20. Seventeen patients had moderate amounts of acid which did not change, or increased less than 20 in the highest two specimens during the first two hours. Of these thirteen did not change during the next three hours and four increased to values each more than 20 but less than values of control tests. Six patients had increases of more than 20 during the first two hours. Of these, during the next three hours two patients decreased, three continued with increase of more than 20, and one (W. W.) reached values, 67 and 62, equal to those of control tests. Two patients during the first two hours reached values which equaled those of control tests: 65 and 73 for patient P. V., 67 and 89 for patient J. G. During the next two hours high values persisted for P. V., 70 and 95, and decreased for J. G., the highest value being 70 and the next highest value, 44.

Of the forty-seven patients tested at one year to six years and eight months after vagotomy and gastroenterostomy, ten had an earlier test in this time

period. The earlier test produced somewhat higher acidity in four and equal acidity in four. There was no free acid in either the earlier or the last test in two patients.

Blood sugars obtained forty-five minutes after insulin in these patients tested at intervals after vagotomy and gastroenterostomy averaged 48 mg. per 100 ml., range 78 to 34.

Fasting Secretions.—Altogether eighty-three of the 120 patients with vagotomy and gastroenterostomy have had determinations of the volume and acidity of twelve-hour overnight collections of gastric content. Of these thirty-nine had preoperative and postoperative determinations. Preoperative volumes averaged 815 c.c., range 3,300 to 73 c.c. Postoperative determinations, early and late, numbered 75. Considered altogether the average postoperative volume was 375 c.c., range 1,115 to 10 c.c. Forty-four patients were aspirated only after vagotomy and their seventy-one tests, early and late, averaged 396 c.c., range 1,990 to 10 c.c.

Of the eighty-three patients tested postoperatively, seven yielded large volumes, 800 to 1,990 c.c., and are considered hypersecreters. In one (M. G.) a volume of 1,095 c.c. occurred six days after vagotomy and subsequent volumes during two years were 300, 64, and 512 c.c. There was no free acid in any specimen from this patient and the first high volume was considered related to an existing malfunction of his gastroenterostomy stoma. Another patient (E. J.) similarly had a high volume six days after vagotomy and gastroenterostomy and not subsequently, insulin test producing little acid. In five patients, vagotomy might be incomplete. Of these, two (F. S. and P. V.) with volumes of 1,420 c.c. and 950 c.c. reached values of free acid during insulin tests of 90 and 106, and 70 and 95, respectively. A third (J. B.) with a volume of 1,990 c.c., free acid 81, increased with the insulin test to values of 57 and 61 during the third and fourth hour. The fourth patient (T. W.) whose volume was 800 c.c., free acid 26, reached high values of 54 and 57 at two and three hours during the insulin test and had large fluctuations of intragastric pressure during gastrometric examinations. The fifth patient (J. M.) is also considered as possibly having an incomplete vagotomy. He had a volume of 1,135 c.c., free acid 33. An insulin test has not yet been performed. A gastrometric study, however, revealed fluctuations of intragastric pressure which ceased when Banthine, 100 mg., was given intramuscularly.

Of the eighty-three patients tested postoperatively, volumes of overnight collections of gastric content have been measured in twenty-five at two to six years, average three years and four months. Average volume was 355 c.c., range 1,990 to 27 c.c. Since this average is somewhat lower than that of all postoperative readings and since examination of the sequence of tests for each of these patients reveals no increase of volume, these observations fail to indicate that there is any increase years following vagotomy and gastroenterostomy.

Values for free acid in terms of clinical units, milliliters N/10 HCl per 100 ml. of gastric juice have been ascertained for the twelve-hour overnight collections of the thirty-nine patients having pre- and postoperative tests. Twenty-five of these patients had no free acid in any of the ninety-five de-

terminations made early and late after vagotomy. Their values for free acid had averaged 39 and ranged from 76 to 0 before vagotomy. Fourteen of the thirty-nine patients had free acid in most of twenty-eight determinations made early and late after vagotomy. Their values for free acid had averaged 47 and ranged from 71 to 15 before vagotomy and averaged 14, range 51 to 0, afterward.

Values for free acid have also been ascertained for the forty-four patients tested only after vagotomy. Thirty-one had no free acid in any postoperative specimens. Thirteen had free acid in most of their postoperative specimens, average 24, range 81 to 0, for 19 determinations, early and late. The patient (J. B.) having 81 is the one described as having a volume of 1,990 c.c. This overnight suction was obtained one year and eight months after vagotomy and the suction five months after vagotomy had obtained 89 c.c. with a free acid of 17. As described, there had been an increase with the insulin test from a control value of 32 to readings of 57 and 61 during the third and fourth hour.

Of the eighty-three patients tested following vagotomy and gastroenterostomy, observations have been obtained in twenty-five two to six years, average three years, after operation. Seventeen had no free acid. Some free acid was present in eight, values averaged 26, range 51 to 10. Examination of the individual sequences for each patient revealed some increase of acidity in the later readings in two, no change of acidity in three, reduction in the later readings in four, and no free acid in any reading in sixteen.

VAGOTOMY AND SUBTOTAL GASTRIC RESECTION

Sixteen patients had both vagotomy and subtotal gastric resection. Vagotomy followed resection in fourteen of these patients who had developed stomal ulcer. Vagotomy preceded resection in two of these patients who developed recurrence of duodenal ulcer following vagotomy performed without drainage. Results described for the sixteen patients include only tests made after both procedures.

Gastrometric Studies.—Six patients had gastrometric studies. Of these three had preoperative and postoperative tests. The average preoperative resting intragastric pressure for the three was 2.2 cm., range 4.0 to 1.0 cm. The average of fluctuations of intragastric pressure preoperatively was 3.0 cm., range 5.4 to 0.6 cm. The average resting pressure for eight tests in these three patients early and late after vagotomy was 3.8 cm., range 6.4 to 1.2 cm. Fluctuations of pressure averaged 1.0 cm., range 2.6 to 0.0 cm. The averages and ranges for the three patients tested only postoperatively were: resting pressure average 2.4 cm., range 2.8 to 1.8 cm., and fluctuations average 1.2 cm., range 2.6 to 0.2 cm. Observations repeated at intervals up to three years revealed no change from the pressures a few weeks after vagotomy.

Insulin Tests.—Of four patients tested during the first three weeks, two developed no acid during the five hours of the insulin test. One had no acid for two hours and then increased less than 20 ml. N/10 HCl per 100 c.c. of gastric juice. One increased more than 20 during the first two hours and also

the next three hours. Four patients were tested at four to seven months. Of these, two developed no acid during the five-hour period, one had no acid for two hours and then increased less than 20, and one increased more than 20 but not to control values during the first two hours and then decreased.

Eight patients were tested one to five years after vagotomy. Two of these patients had single tests and each had no free acid during five hours. Five patients had two tests in this time period. Of these there was no free acid in either test of two. The earlier test produced higher values in one and the second test higher values in two. In one of the two (C. P.), the second test was three years after vagotomy and the higher values, 65 and 67, occurred during the first two hours and equaled those of control tests. However, during the next three hours there was no free acid. The eighth patient (M. W.) had seven insulin tests. Two large stomal ulcers had developed after resection and healed slowly. Scar tissue developed and obstruction occurred and later required surgical repair. The first vagotomy was incomplete as judged by a second operation during which overlooked vagal fibers were found and removed. The insulin test eleven days after the first and incomplete vagotomy produced high values of 43 and 58 during the first two hours and 52 and 53 during the next three hours. A second test four months later produced values of 47 and 54 during the first two hours but there was little or no acid during the next three hours. Nine months later the second vagotomy was performed and twenty-three days afterward there was no acid in eight of ten half-hour specimens, a single reading at the end of two hours being 41 and one reading in the three-hour period being 40. Three months later there was no free acid in any specimen during the five readings. In three subsequent insulin tests performed at intervals during two years after the second vagotomy there were, consecutively, an increase in only one specimen in the first two hours, 46, an increase in a single specimen during the three-hour period, 42, and an increase to 35 in the first two hours and 51 and 62 during the three-hour period. It is interesting that the seven tests in this patient with vagotomy and resection did not produce any two readings in any five-hour period equaling those of the tests in control ulcer patients.

Fasting Secretions.—Measurements of volume and acidity of twelve-hour overnight collections of gastric juice were obtained in six patients before and after vagotomy and in five patients afterward, only. In the six, the preoperative volume averaged 634 c.c., range 250 to 68 c.c. Free acid values averaged 24 ml. N/10 HCl per 100 c.c. of gastric juice and ranged from 55 to 5. Postoperatively the average volume for seventeen determinations in these six patients was 299 c.c., range 650 to 45 c.c. Postoperatively free acid was not present in any of the seventeen specimens. The volumes of the five patients with overnight collections obtained only after vagotomy averaged 353 c.c., range 673 to 36 c.c. Three of the five patients had no free acid during any test. One had a value of 50 three years after vagotomy and at this time the volume was 100 c.c. The fifth patient tested five times during three years had consecutive values of 0, 22, 0, 26, and 15.

VAGOTOMY FOR GASTRIC ULCER

Of nine patients treated for gastric ulcer, four had vagotomy alone, two vagotomy and pyloroplasty, two vagotomy and gastroenterostomy, and one vagotomy followed nine months later by subtotal gastric resection.

Gastrometric Studies.—Five patients, four with vagotomy alone and one with vagotomy and gastroenterostomy, were tested. Average resting total intragastric pressure for eight tests three weeks to two years after vagotomy was 3.4 cm., range 5.4 to 2.2 cm. Average of fluctuations of pressure was 0.4 cm., range 0.8 to 0.2 cm.

Insulin Tests.—Three patients, two with vagotomy alone and one with vagotomy and pyloroplasty, were tested during the two weeks after vagotomy; no free acid appeared in the two- or the three-hour period. One patient with vagotomy alone was tested at four months and there was no acid during the five hours. Two patients were studied at two to five years. One tested only at five years had an increase of less than 20 in the five-hour period. The other patient had a test at two years with no free acid in any specimen, but at three years and five months had two single readings, each 32; the remainder of the specimens during the five-hour period contained no free acid.

Fasting Secretions.—Measurements of volume and acidity of twelve-hour overnight collections of gastric juice were obtained before and after vagotomy in two patients and afterward, only, in three. The preoperative volumes of the two were 650 c.c. and 400 c.c. and the values for free acid were 15 and 27. Considering all postoperative values for the five patients together there were seven determinations and the average was 347 c.c., range 850 to 20 c.c. There was no free acid in any of the seven collections.

RESULTS OF USE OF BANTHINE OR CAFFEINE DURING GASTROMETRIC AND SECRETORY STUDIES

As previously reported[6] six of the 175 patients (J. F., T. W., P. V., C. M., S. S., and L. C.) are considered as having recurrence of ulcer and another two (M. W. and E. A.) delayed healing of jejunal ulcers. Each of these patients is now taking Banthine. Routine gastrometric and secretory tests alone have not been too satisfactory in determining completeness of elimination of vagal pathways or incomplete vagotomy as an explanation of recurrence. Accordingly, studies have been undertaken recently to determine what the effects of injection of Banthine or of caffeine and sodium benzoate would be.

Gastrometric studies supplemented by injection of Banthine or of caffeine have been obtained in four of the six patients with recurrence, and in two patients with highly acid secretions but without symptoms. Three of the six patients (P. V., T. W., and J. M.) had strong fluctuations of intragastric pressure and highly acid secretions. In each the strong fluctuations of intragastric pressure ceased immediately after intramuscular injection of 100 mg. of Banthine and remained quiescent an hour or longer. A typical tracing is shown in Fig. 1. One of the six patients (J. F.) had strong fluctuations of intragastric pressure and after intramuscular injection of 0.5 Gm. of caffeine

and sodium benzoate developed a large contraction at three minutes and a tonus contraction two minutes later. In these four patients it would seem that parasympathetic block or, conversely, stimulation by drugs has evidenced failure of complete interruption of parasympathetic pathways by surgery. The fifth patient (J. G.), during his insulin test, developed values for free acid well within the control range for ulcer patients. Nevertheless, there were no forceful waves during his motility test or following the injection of caffeine and sodium benzoate (Fig. 2). Since this patient has no symptoms of ulcer it is possible that parasympathetic motor pathways have been interrupted by surgery and that the high secretions continue by some other mechanism. Whatever the explanation, it is evident that in this patient results of gastrometric and insulin tests did not agree. The sixth patient (C. M.) had mild distress and had had two episodes of moderate gastrointestinal bleeding. Symptoms developed

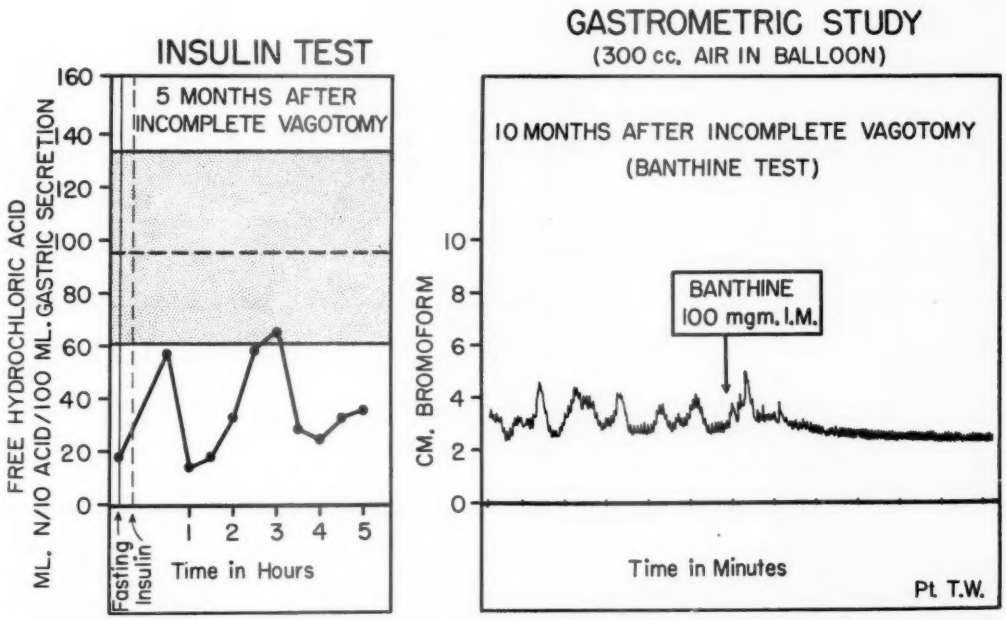

Fig. 1.—Five months after vagotomy insulin hypoglycemia was associated with increase of free acid; one reading is within the shaded area representing the range of control insulin tests in ulcer patients. Ten months after vagotomy forceful fluctuations of intragastric pressure were evident during gastrometric study. Incomplete interruption of parasympathetic nerve pathways seems confirmed since injection of Banthine interrupted these abnormally high gastric contractions. This patient had recurrence of ulcer.

three and one-half years after vagotomy performed for a jejunal ulcer which had followed previous gastroenterostomy. During his insulin test at three and one-half years no free acid developed in any specimen. Also during gastrometric studies there were no forceful fluctuations of intragastric pressure. Injection of caffeine and sodium benzoate produced no significant change of the motility pattern (Fig. 3). It would seem that these insulin and motility tests confirm each other in evidencing completeness of surgical interruption of the parasympathetic nervous pathways and that the reason for recurrence of hemorrhages remains unexplained. No ulcer was found at a secondary

operation. An additional nineteen patients have recently been tested at intervals after vagotomy. In each, fluctuations were low or absent and caffeine produced no change.

Two patients had hypersecretion four and ten months after vagotomy, evidenced by four control fifteen-minute aspirations after a twelve-hour period of fasting, and were then given 100 mg. of Banthine. There was no reduction of free acid in ten subsequent aspiration specimens. A third patient similarly tested and with similar hypersecretion decreased to no free acid after injection of Banthine. It would seem that the hypersecretion in two was not dependent upon overlooked vagal pathways but that in the third, surgical interruption of the parasympathetic nerves may have been incomplete.

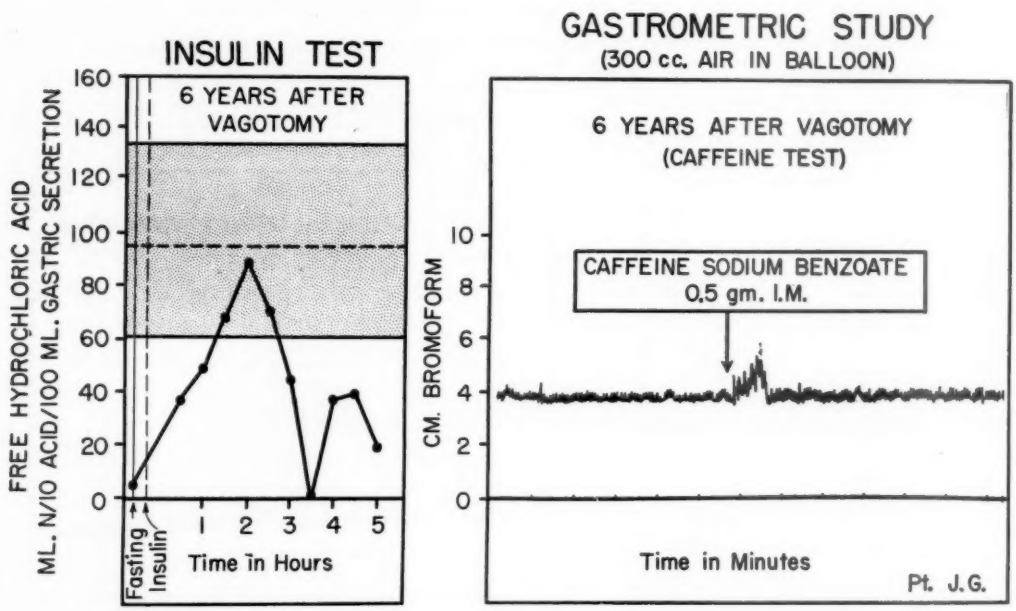

Fig. 2.—Six years after vagotomy insulin hypoglycemia was associated with increase of free acid; three readings are within the shaded area representing the range of control tests in ulcer patients. Gastrometric study at this time revealed minimal fluctuations of intragastric pressure and no significant response to injection of caffeine. The gastrometric-caffeine study suggests that parasympathetic pathways have been interrupted although the insulin test is "positive." This patient has no symptoms of recurrence of ulcer.

One patient (L. C.) among the six considered as having recurrence of ulcer[6] and one (E. A.) of the two with delayed healing of jejunal ulcer have not as yet been described in connection with any gastrometric or secretory study in this report. The patient with recurrence (L. C.) had only one test, showing an overnight suction with a value of 50 for free acid and a volume of 100 c.c. The second patient (E. A.) had an overnight suction volume of 257 c.c. with no free acid ten days after vagotomy. Seven months later he had an insulin test with values for free acid of 59 and 42 during the three-hour period.

SUMMARY AND DISCUSSION

Of the 175 patients, gastrometric or secretory tests or both have been made in 150. Gastrometric studies were made in 86 control patients with duodenal

ulcer. Average resting intragastric pressure, or tone, was 2.2 cm. of bromoform and average of fluctuations, or contractions, was also 2.2 cm. Gastrometric studies were made at intervals after vagotomy in sixty-seven patients, not including those with subtotal gastric resection. Average resting intragastric pressure, or tone, for sixty-three patients was 3.3 cm. and average of fluctuations was 0.4 cm. Postoperative records of the remaining four patients in this group, 5.9 per cent, definitely varied from the uniform pattern of increase of tone and decrease of contractions. The average resting pressure for the four was 3.9 cm., and the average of fluctuations was 3.1 cm.

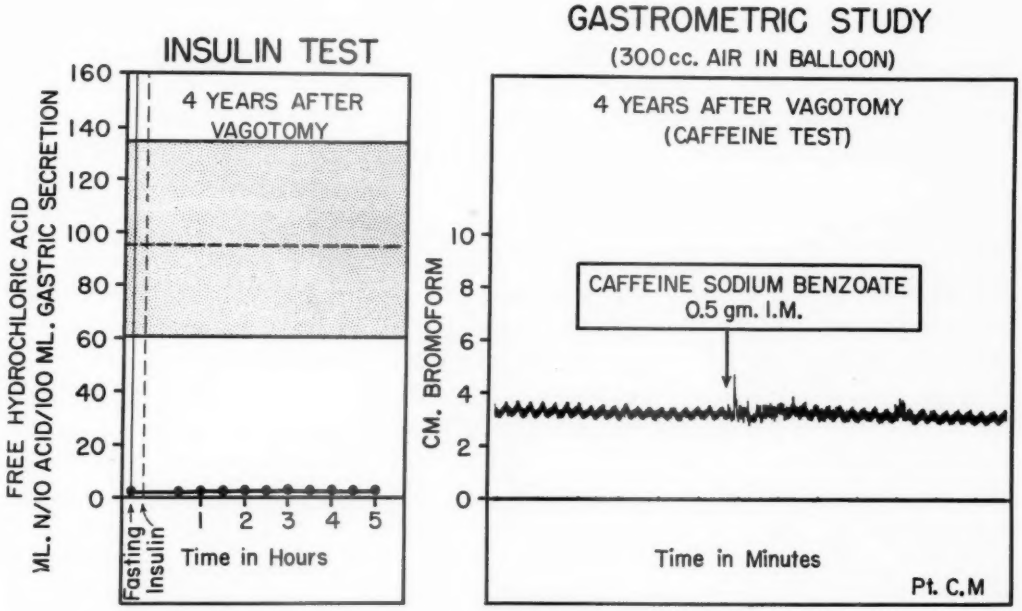

Fig. 3.—Four years after vagotomy insulin hypoglycemia produced no free acid. Gastrometric study revealed low fluctuations of intragastric pressure and no increase with injection of caffeine. Both tests suggest that parasympathetic pathways have been interrupted.

Of the tests employed, the gastrometric method described seemed easiest to interpret. Occurrence of fluctuations of intragastric pressure approaching the average of the control patients, 2.2 cm. of bromoform, seemed to strongly suggest incomplete vagotomy. Of the four patients showing this reaction among the sixty-seven tested three had definite recurrence of ulcer. Of the sixty-three patients whose fluctuations after vagotomy did not reach 2.2 cm. of bromoform only one had a mild recurrence of ulcer and his fluctuations were somewhat high, 1.8 cm. Interpretation of the gastrometric tests was facilitated by the intramuscular injection of 100 mg. of Banthine during the period of observation if contraction waves seemed somewhat high, or the injection of caffeine if contraction waves seemed low. Apparently Banthine arrested contractions if the parasympathetic nervous system had not been completely interrupted and the stimulation of contractions by caffeine failed if vagotomy had been complete.

TABLE I. PERCENTAGE DISTRIBUTION OF PATIENTS ACCORDING TO FREE ACID IN LATEST TESTS (THREE MONTHS TO SIX YEARS AND EIGHT MONTHS AFTER VAGOTOMY, AVERAGE THREE YEARS)

FREE ACID, CLINICAL UNITS†	INSULIN TESTS*				12 HOUR OVERNIGHT SUCTIONS			
	CONTROL ULCER GROUP	VAGOTOMY, GASTROENTER-OSTOMY	THORACIC VAGOTOMY ALONE	VAGOTOMY AND RESECTION	CONTROL ULCER GROUP	VAGOTOMY, GASTROENTER-OSTOMY	THORACIC VAGOTOMY ALONE	VAGOTOMY AND RESECTION
121-130	12							
111-120	8							
101-110	18							
91-100	12‡							
81-90	18	2			1	1		
71-80	12	3			5			
61-70	20	4		14	14			
51-60		8	15	14	16	1		
41-50		4	12		17‡	3	3	9
31-40		6	12	15	13	5	13	
21-30		16	15‡		12	6	3	
11-20		10‡	23		12	6	11	10
0-10		47	23	57‡	10	78‡	70‡	81‡

*Patient distribution is according to average of the highest two readings following insulin.
†Milliliters of N/10 hydrochloric acid per 100 milliliters of gastric juice.
‡Mean.

Of the 175 patients studied clinically, insulin tests were performed in 124, not including the patients with gastric ulcer. Control insulin tests were performed in twenty-four patients with duodenal ulcer and without surgery. Tests were continued five hours after the injection of insulin. The average value for free acid in the highest two readings for each control patient was 94, range 133 to 58. Of the 124 patients tested at intervals after vagotomy, seventeen, 13 per cent, had two high readings in the control range. Of the seventeen patients, four had recurrence of ulcer. Among the remaining 112 whose values were below those of control patients, two had delayed healing of stomal ulcer and developed obstruction by scar tissue; one had unexplained mild bleeding, low acid and motility, and a negative exploratory operation. These three patients did not necessarily have incomplete vagotomy. It would seem apparent, therefore, that failure to increase free acid to control values during a five-hour insulin test gives encouragement that recurrence of ulcer is unlikely, and that increase to control values does not suggest a chance of recurrence greater than 4 in 17.

Of the 175 patients studied clinically twelve-hour overnight collections of gastric juice were obtained in 129, not including those with gastric ulcer. Control observations were made in seventy-five patients whose average volume was 784 c.c. and average value for free acid 41. For 119 of the 129 patients tested, the average volume was 321 c.c. Postoperative volumes of the remaining ten patients in this group, 7.7 per cent, seemed excessively high, averaging 1,119 c.c., each patient exceeding the average, 784 c.c., of the control patients. Only one of the ten patients developed recurrence. Recurrence developed in two of the 119 patients tested who did not have volumes as high as 784 c.c. The average value for free acid for 127 of the 129 patients tested including those with no free acid was 5.8. Postoperative values for the remaining two patients in this group, 1.5 per cent, seemed excessively high, 81 and 50, each patient exceeding the average value, 41, of the control patients. One of these two patients has had a recurrence. Recurrence developed in two of the 127 patients tested who did not have amounts of free acid as high as 41. It, therefore, seems apparent that high amounts of free acid are more significant than high volumes of secretion in estimating the likelihood of recurrence.

Of the 150 patients tested by one or more methods the latest study by at least one method has shown an aberrant observation approaching control figures in twenty-seven, or 18 per cent. However, the review of all tests now completed and the clinical evaluation of the entire group of 175 patients[6] gives us the general impression that the percentage of patients with incomplete vagotomy more closely approaches the 4.5 per cent determined by gastrometric studies than the 13 per cent determined by our method or using the insulin test, the 7.7 per cent determined by excessive volume of twelve-hour overnight collections of gastric juice, or the 1.5 per cent for excessive amounts of free acid in these collections.

We have found no evidence during gastrometric studies that there is any tendency toward return of contractions or decrease of tone during the years following vagotomy. Occasionally contractions increased, or decreased slightly,

but usually they remained low. This observation also holds true for the insulin tests and the twelve-hour overnight suctions. The average of the latest two readings for each patient during insulin tests and the value for free acid in overnight suctions have been used as the basis for calculations of the percentage distribution of patients according to acidity presented in Table I. It is evident from the material presented in this paper, as well as from examination of the distribution of patients according to the average of the two highest values for free acid of the insulin tests, Table I, that results can well be interpreted according to whether each of the two highest values during the five-hour period fall into the range of the values for the control ulcer patients, 58 to 133. Also it is evident that results of twelve-hour overnight collections of gastric juice can well be interpreted according to whether values for free acid equal or exceed the average value for control collections, 41.

CONCLUSIONS

1. Effects of vagotomy upon gastric motility and acidity have persisted during observations up to six years and eight months.

2. A gastrometric method of study supplemented by the injection of Banthine or of caffeine is introduced as a method for testing completeness of interruption of parasympathetic nerve pathways following surgery.

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DISCUSSION

DR. F. D. MOORE.—I would like to congratulate Dr. Grimson and his group who, right from the start in the vagotomy sweepstakes, have been way out in front because they have been studying facts, they have been following their patients carefully, and they have not been swinging back and forth with the pendulum of public opinion. We also feel that vagotomy, now after about six or seven years in our hands, is worth a good, careful second look. A lot of the patients are doing remarkably well with vagotomy and nothing else, which is a beautifully simple surgical therapy for ulcer.

I would like to make just two points. One, a clinical point in corroboration of what has been said, but maybe with an added twist: We have seen patients with perfectly flat insulin tests six years after vagotomy (which is very gratifying to the surgeon) where, by x-ray, the motility is still inhibited. Yet, in several, we have found an active, recurrent duodenal ulcer with a crater demonstrable pathologically at gastric resection. There must be another activation pathway, in addition to the parasympathetic and the antral humoral mechanism. I believe that the recent work of Gray at our hospital suggests what that pathway is. He has taken duodenal ulcer patients and given them either ACTH or cortisone and it takes a long time, it does not happen fast—it takes three weeks, four weeks, five weeks—then their acidity goes up, their urinary excretion of uropepsin goes up, and they get symptoms. What is the mechanism? What pathway is being followed?

I do not know, but that pathway, whatever it is, by which steroids affect parietal-cell function is not dependent upon the parasympathetic because the same effects on gastric secretion and on the urinary excretion of uropepsin are observed following long administration of ACTH and cortisone in patients with complete vagotomy. I believe that gives us all something to think about.

DR. GRIMSON (Closing).—I want to thank Dr. Moore for his comments about our studies and his prediction that vagotomy with gastroenterostomy deserves a "second look." Also I would like to agree again with his conclusions and ours of four years ago that vagotomy without a drainage procedure should be abandoned. Studies, then and now, reveal that there are patients who have done well after vagotomy alone. However, the incidence of trouble, gastric retention, and recurrence of ulcer is too high, and vagotomy should always be accompanied by some form of gastroenterostomy. Subtotal gastric resection is also accompanied by a gastroenterostomy. Whether the surgeon elects to eliminate the cephalic or neurogenic factors of ulcer by vagotomy, or the antral or chemical digestive factors by subtotal gastric resection, drainage is necessary since many patients requiring operation have partial or marked obstruction.

Dr. Moore is correct in emphasizing the fact that injection of histamine or stimulation of naturally occurring gastrin from the antrum will activate secretions by a process similar to that occurring during the second stage of digestion as long as some or most of the acid-producing fundus of the stomach remains intact, and even though the vagus has been eliminated. Similarly, gastric secretions can be activated and ulcer caused by a neurogenic process similar to that occurring during the first stage of digestion as long as the vagus and fundus remain intact and even though the antrum and distal half or two-thirds of the

stomach has been removed. Fortunately, either vagotomy with gastroenterostomy or subtotal gastric resection usually prevents recurrence of ulcer. Only infrequently would it be necessary to handicap patients by eliminating these two digestive mechanisms and adding the side effects characteristic of each of the two operations.

I would like to express appreciation for the interest and tolerance with which this society has accepted studies of vagotomy. It is reassuring to know that members are using vagotomy, some only occasionally and some frequently. Discussions of effects of vagotomy and of resection have been stimulating. With close competition, surgeons of both schools of thought seem to be giving greater attention to the pre- and postoperative management and searching for methods of improving results. In my opinion, results of subtotal gastric resection are usually good and approach the effectiveness and safety of vagotomy with gastroenterostomy. With either procedure some patients experience troublesome side effects and a few, recurrence of ulcer. There seems to be no decisive decision or universal agreement as yet on the preferable procedure for use when conditions warrant choice of one operation or the other. However, acceptance of vagotomy by most surgeons for certain of the more difficult problems of ulcer, and acceptance of vagotomy as the preferable procedure for complicated duodenal ulcer by a growing minority is a situation I would like to acknowledge.

THE SIGNIFICANCE OF THE SYMPATHETIC NERVOUS SYSTEM IN ACUTE CHOLECYSTITIS

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CLINICAL and experimental investigations have emphasized the significance of certain mechanical and chemical factors in the etiology of cholecystitis.[16, 18, 49, 50] These factors, involving obstruction of the cystic duct and derangements in bile constituents, are now generally believed to play the most important roles in initiating inflammatory changes in the gall bladder.

More recently, interest has been aroused in the significance of the nervous mechanism in the pathogenesis and progression of the disease. The basis for this interest lies in observations suggesting that the nerve supply to the gall bladder and extrahepatic duct system may be concerned in the production of smooth-muscle spasm and secondary vascular obstruction, with consequent progression and accentuation of the ischemic and inflammatory process. Womack has indicated the extent to which this nerve supply may be involved in inflammatory lesions of the gall bladder. Further evidence of this relationship is provided by certain observations on the sympathetic nervous system in pancreatitis. A number of observers have directed attention to the effectiveness of splanchnic block and splanchnic section in the treatment of both acute and chronic pancreatitis.[12, 13, 17, 28, 29, 32, 34, 35, 37, 39] We, too, have been impressed by the dramatic relief of pain and the striking improvement in clinical manifestations following this procedure. The similarity in pain and pain pathways in pancreatic and cholecystic diseases and their frequent association would suggest that this form of treatment might also be effective in acute cholecystitis. That this is true has been recently reported by Bonnet,[3, 4] and by Eastwood and Womack.[15] On the basis of these observations the present experiment was undertaken in an effort to study the effect of interruption of the appropriate sympathetic pathways on the pathogenesis of acute cholecystitis.

CLINICAL AND EXPERIMENTAL OBSERVATIONS

The first part of the study was concerned with clinical observations on the effect of splanchnic block using 1 per cent procaine hydrochloride solution in six patients with acute cholecystitis, the diagnosis being confirmed in each instance by subsequent laparotomy. The results were similar to those obtained in acute pancreatitis with almost immediate and complete relief of pain in all cases, confirming the report of previous investigators.[3, 4, 15] Although, theoretically, both sides should be blocked, actually blocking only the right side was

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sufficient in some cases. In others this provided incomplete relief of pain and the left side was then injected, resulting in complete abolition of pain. Because sympathetic block was used in these cases only during the immediate preoperative period, the duration of pain relief beyond three hours following the block has not been ascertained. For this period, however, and without exception, there was definite and complete relief of pain.

The second phase of the investigation consisted in studying the effect of sympathectomy on the progression of experimental acute cholecystitis. The dog was used as the experimental animal. The control study consisted of a transthoracic exposure of the gall bladder under Pentothal Sodium anesthesia, endotracheal aeration, and sterile technique. Without manipulating the gall bladder, the cystic duct was carefully separated from the adjacent artery and vein and ligated with fine silk. Ten cubic centimeters of bile salts (2 Gm. sodium dehydrocholate) were then injected through the cystic duct into the gall bladder. A second ligature around the cystic duct then prevented leakage so that, following injection, the gall bladder remained tense. Such an injection proved necessary as simple occlusion of the cystic duct of the dog, without injection, did not result in acute cholecystitis. This method of producing acute cholecystitis is basically similar to that previously used by a number of investigators who found that the gross and microscopic changes in the gall bladder wall produced by this means closely resembled those occurring in human cholecystitis.[1, 18, 38, 40, 50]

Postoperatively, the animals were given oral feedings as tolerated. During the following week, the animals were sacrificed at periods of two days, four days, and seven days, respectively. The gall bladder was then described, color photographs taken, and histologic study made of the fundus. The cystic artery was inspected for signs of injury or ligation so that primary infarction of the gall bladder could be excluded. On the basis of the gross and histologic findings the gall bladders were classified into one of the following categories: (a) normal, (b) minimal or early cholecystitis, showing distention, edema, but no exudate nor signs of ischemia or gangrene, or (c) advanced cholecystitis showing signs of impending or early gangrene. Twenty-seven dogs were used as controls.

A second group of twenty-eight dogs was studied in the same manner except that at the time of ligation and injection, a right sympathectomy was performed by resecting T_6 through T_{12} including the splanchnic nerves.

The third group of sixteen dogs had bilateral sympathectomies, the one on the left being performed first. Five days after the left sympathectomy, the right chest was opened, sympathectomy performed, and ligation and injection of the cystic duct were done as described previously.

RESULTS

Control Group.—In the twenty-seven control experiments the gall bladder appeared normal in only four instances (15 per cent) (Table I). These four gall bladders remained distended as they had been immediately after ligation and injection but showed no other sign of inflammation. Nine of the gall

Fig. 1.—Color photograph of gall bladder of one of the control animals showing typical inflammatory changes of acute cholecystitis with marked edema, serosal exudation, and areas of hemorrhage and necrosis.

Fig. 2.—Color photograph of gall bladder of dog with no inflammatory changes following bilateral sympathectomy and the procedure used in the control animals to produce acute cholecystitis.

bladders (33 per cent) showed minimal progression of inflammatory changes, manifested chiefly by the edema and occasional areas of leukocytic infiltration. Fourteen of the animals (52 per cent) showed signs of progression of the cholecystitis to the stage of impending or early gangrene (Fig. 1). The gall bladders were not only edematous but had areas of hemorrhage, mucosal necrosis, serosal exudate, or areas of necrosis of the entire thickness of the gall bladder wall with an occasional perforation.

TABLE I. EFFECT OF SYMPATHECTOMY ON THE PROGRESSION OF ACUTE CHOLECYSTITIS

		NORMAL GALL BLADDER		MINIMAL CHOLECYSTITIS		ADVANCED CHOLECYSTITIS	
	TOTAL NO. DOGS	NO. DOGS	PER-CENTAGE	NO. DOGS	PER-CENTAGE	NO. DOGS	PER-CENTAGE
Control	27	4	15	9	33	14	52
Right sympathectomy	28	16	57	7	25	5	18
Bilateral sympathectomy	16	12	75	3	19	1	6

Right Sympathectomy Group.—Of the twenty-eight animals in which right thoracic sympathectomies were performed at the time of ligation and injection, sixteen (57 per cent) showed normal gall bladders, seven (25 per cent) minimal cholecystitis, and five (18 per cent) advanced cholecystitis (Table I). The inflammatory changes in the latter five gall bladders were as advanced as any in the control group.

Bilateral Sympathectomy Group.—Of the sixteen dogs which had bilateral sympathectomies, twelve (75 per cent) revealed normal gall bladders (Fig. 2), three (19 per cent) showed slight inflammatory changes, and one (6 per cent) showed advanced inflammation (Table I).

DISCUSSION

It is apparent from these observations that interruption of the sympathetic pathways to the gall bladder and extrahepatic duct system produces a significant effect upon the inflammatory process in the gall bladder, with at least prompt relief of pain in human beings and subsidence or arrest in progression of the inflammatory process in a high proportion of instances in dogs. The fact that bilateral sympathetic denervation provided an even greater effect in protecting against the development of cholecystitis than unilateral (right) sympathectomy would seem to add to the significance of this phenomenon. The latter finding suggests that the more complete the denervation, the more effective is the procedure, thus giving greater meaning to its role in this process. The exact mechanism by which this takes place is not entirely clear since the precise actions of the extrinsic nerves upon biliary tract function in man have not been definitely established. There is little, if any, evidence that the autonomic nervous system plays a direct role in regulating the normal function of the gall bladder in man. Vagal stimulation produces contraction of the gall bladder in animals,[22, 43, 46, 51] but the contraction and emptying of the human gall bladder is almost entirely under hormonal control.[5, 6, 21, 22, 44]

The sympathetic nervous system is the sensory pathway for the gall bladder. Excellent studies reveal the pain pathways from the gall bladder of both the dog and man to be the sympathetic chains, T_6 to T_{12} by way of the splanchnic nerves and celiac ganglia.[3, 4, 7, 9, 14, 15, 19, 20, 23, 25, 26, 30, 42, 45, 49] Although the sympathetic innervation of the biliary tract is bilateral, most of the pain pathways traverse the right side.[2, 10, 19, 33, 36, 41] After bilateral sympathectomy Ray and Neill were unable to produce pain in the unanesthetized patient by distention of the gall bladder. Relief of pain in chronic biliary tract disease by splanchnic block or splanchnicectomy has been reported by a number of observers.[3, 4, 8, 11, 19, 24, 25, 27, 30, 31, 47, 51] That it is also effective in relieving pain in acute cholecystitis is demonstrated by the results obtained in the present study and by the work of Bonnet[3, 4] and of Eastwood and Womack.[15]

Although interruption of the appropriate sympathetic pathways may have therapeutic value in acute cholecystitis, it probably has little diagnostic significance since the same procedure relieves the pain of acute pancreatitis and possibly the pain resulting from inflammation of other viscera. Perhaps, as suggested by Eastwood and Womack, it may have diagnostic value in differentiating biliary tract pain of organic origin from that occurring in psychoneuroses. The use of such a procedure for relief of pain might be an adjunct to surgical therapy in instances where operation must be postponed. It might also prove a valuable adjunct in the treatment of the occasional patient in whom operative intervention is considered ill advised. Potential dangers of pain suppression by this method are, of course, realized and require further investigation.

While it is apparent from this experiment that sympathetic block alters the progression of acute cholecystitis in dogs, it cannot be inferred that the same thing happens in human beings. Perhaps it does, but experimental cholecystitis in the dog may not simulate the development of the disease in man, despite the fact that the gross and microscopic features of the lesions are similar. There is reason to believe, however, from the excellent studies of Womack, Mallet-Guy, Gage, and de Takats, that interruption of the nerve pathways to this region, with the blocking of impulses arising from the stimulating action of the visceral distortion or inflammatory process upon the nerve endings and the abolition of resultant autonomic reflexes, may have a beneficial effect upon the subsidence of smooth-muscle spasm and vasoconstriction and, consequently, upon the progression of the inflammatory process itself. Obviously, further investigations along these lines are required to clarify this mechanism, but the results of these and other studies strongly suggest a significant relationship.

SUMMARY

1. In six patients with acute cholecystitis, the diagnosis being confirmed in all by subsequent laparotomy, procaine splanchnic block produced prompt and complete relief of pain.

2. Sympathetic denervation of the nerve supply to the gall bladder and biliary tract in the dog has a significant effect upon the inflammatory process in experimental acute cholecystitis produced by ligation of the cystic duct and

the introduction of bile salts into the gall bladder. Whereas in the control series only 15 per cent of the animals had normal gall bladders following this procedure, in the animals having a simultaneous right sympathetic denervation this figure was 57 per cent, and in those with bilateral denervation it was 75 per cent.

3. The underlying mechanism of these effects is not entirely clear, but the belief is expressed that it may be concerned with the blocking of impulses arising from the stimulating action of the visceral distortion or the inflammatory process upon the nerve endings and the abolition of resultant autonomic reflexes, thus producing a beneficial effect upon the subsidence of smooth-muscle spasm and vasoconstriction and consequently upon the progression of the inflammatory process itself.

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DISCUSSION

DR. B. S. RAY.—As you know, we have been interested in visceral sensation following sympathectomy and have made rather extensive studies on this subject. Our studies with regard to the biliary tract had to be done through the open abdomen and we felt that these were rather more appropriate than some of the studies we had to make at long distance with balloons in the intestinal tract, so that we felt quite sure about our findings in the biliary tract. We were, at first, led to believe by previous work, particularly that of Davis, that the innervation of the biliary tract was unilateral, but it was very evident to us that it was bilateral; and Dr. De Bakey has brought this out very nicely in his studies. I do not believe I was able to tell from his report whether his unilateral injections had all been on the right side. My guess is that it is about equal and that it is not dominantly on the right. Among people who have written on the innervation of the pancreas, there have been those who maintain that one side was important to the exclusion of the other or that one side was dominant; and, in the reported cases, you will find that some say they have cured pancreatitis—the pain of pancreatitis—with left-sided injections, and others with injections on the right side. I think the fact remains that sometimes a partial interruption on one side or the other of the visceral innervation is enough to control the individual patient's complaint of pain. With regard to the development of cholecystitis, perhaps one way to get at this problem would be eventually to study the incidence of cholecystitis in patients who have had thoracolumbar sympathectomy, and there are certainly a great many of these patients. Our own series is about 600 and I think everyone of us with a reasonably large series would be quite willing to cooperate in such a study. You could then compare the incidence with what the accepted might be in the unsympathectomized patients. We became concerned over the possibility that some of our patients who already had gallstones might develop unrecognized cholecystitis after we had sympathectomized them for hypertension, so that we established a rule of studying the gall bladder by cholecystograms before sympathectomy in any patients who were suspect. I don't know how strictly we have stuck to that. We availed ourselves of the opportunity to make our studies originally on those patients who had gallstones and who were coming up for sympathectomy. To my knowledge, we have not had any of the patients in our 600-odd sympathectomies who have developed acute cholecystitis. I believe there are one or two who had their gall bladder removed for indigestion, principally eructations and not pain, but I know of no development of acute cholecystitis.

PROFESSOR RENÉ LERICHE discussed this paper in French. Interpretation by Dr. Mark M. Ravitch: I wish Dr. De Bakey had interested Prof. Leriche in a simpler subject. The Professor said he was much interested in the communication of Dr. De Bakey, and that it confirms ideas which he had long had concerning the part that the vegetative nervous system played in the pathological clinical picture of disease states. He exclaims in distress that the pathologists have almost never studied the condition of the vegetative nervous system from the pathologic anatomic standpoint in diseases. If they had, and when they do, they would discover lesions, and he described "neuromas of cicatrization." He says that it is important for us to study the vegetative nervous system by all the techniques at our disposal so as to know the causes of disease. He says there are a good many diseases which we accept as diseases with unknown causes. For instance, and I don't know to whom he was addressing this, surgeons have for years amused themselves with the problem of intestinal invagination, describing the numerous folds, back and forth, of the intestine. He says that is not the problem. The thing to do is to get at the heart of the problem. Why do these patients have invagination? In that way, we can learn something about them—and, actually, he has studied, in one case of intussusception, the plexuses of Meissner and Auerbach and discovered very gross lesions there. In acute and chronic cholecystitis, he has found lesions of the

parietal vegetative nervous structures and, similarly, in peptic ulcer there are frequently found lesions in the sympathetic plexuses. He says there is a tremendous lacuna in our knowledge of disease in general and this is one important aspect of that lacuna. In confirmation of Dr. De Bakey's work, he again says that this demonstrates the clinical applicability of these theories and he has himself a number of times been able to transform red-hot cholecystitis into cold cholecystitis and to operate at his leisure when the process had subsided as a result of splanchnic block.

DR. HAROLD A. ZINTEL.—Inasmuch as the question has been raised, I would like to say that in a series of 100 of our patients who had thoracolumbar sympathectomy, two patients have developed acute calculous cholecystitis. One was just in the hospital very recently and he had a gangrenous gall bladder. Pain was not a predominant symptom in this case. I think it would be most interesting to collect the data of the patients who have had thoracolumbar sympathectomy from the various clinics and to determine what the incidence of cholecystitis in these patients has been.

DR. DE BAKEY (Closing).—I would like to express my grateful appreciation to the discussers of this paper and, particularly, to Professor Leriche with whom I had a very delightful year of study. In fact, I am indebted to him for stimulating my interest in the study of the sympathetic nervous system in addition to the inspiration to do work in this field. With regard to comments by Dr. Ray, our experience would indicate that blocking the right side first (and that is what we do first) often gives sufficient relief of pain to the patient, at least subjectively, so that he does not require additional injections. But I am inclined to believe from our experience with the need for doing bilateral injections that Dr. Ray is correct in the belief that there is bilateral innervation, at least sufficient bilateral innervation to be of considerable significance. We have had the same experience in acute pancreatitis except that in acute pancreatitis we block the left side first. Here again we have found that very often the unilateral block on the left side provides sufficient relief of pain so that it becomes unnecessary to do bilateral blocks. In a significant number of cases, however, the bilateral block is necessary to produce complete relief of pain.

ARTERIOVENOUS FISTULAS AND ARTERIAL ANEURYSMS

The Repair of Major Arteries Injured in Warfare, and the Treatment of an Arterial Aneurysm With a Vein Graft Inlay

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IT IS generally held that in the presence of an adequate collateral blood supply the most effective treatment of an arteriovenous fistula is quadruple ligation and excision. Numerous tests have been devised to measure the adequacy of the collateral circulation before and during operation.[1-7] These methods give valuable information about the prospect of viability in the extremity after ligation of the major vessels but do not accurately assess the possibility of normal function. Despite these observations, obliteration of a fistula or an aneurysm is not infrequently followed by claudication or a feeling of coldness in the extremity, indicating poor nutrition.[8-13] The fact that viability is usually preserved but normal function is not, has led to the development of techniques which preserve arterial continuity.[8, 12, 14-16, 28]

Matas credits Murphy with recording the first successful union of an artery after circular resection of the injured area.[17] Matas, himself, changed the whole concept of the treatment of aneurysms by introducing his reconstructive and restorative endoaneurysmorrhaphy.[14, 15] Bickham, following Matas' lead, introduced transvenous repair of the arterial defect in arteriovenous fistula.[8] Freeman, who reviewed the subject recently, succeeded in restoring arterial continuity in eighteen lesions involving major arteries.[12]

A number of objections to arterial repair have been raised. Bigger emphasized the danger of suturing calcified vessels.[9] Others have stressed the difficulties of mobilizing the vessels sufficiently for suture, or have objected to the method of transvenous repair for fear of overlooking other damaged portions of the vessels.[18] A review of a number of the frequently cited instances of complications following restoration of arterial continuity reveals that most often they have occurred in fistulas of long standing in which there were degenerative changes in the arterial wall.

Reid reported a patient operated upon by Halsted in 1916—a 48-year-old man who had an ateriovenous fistula in Hunter's canal for more than thirty years.[19] The proximal artery was dilated to the heart, and just below Poupart's ligament it was very tortuous. Halsted divided the artery and vein, establishing continuity in both with silk sutures. Six years later the patient returned with an aneurysm in Scarpa's triangle and a gangrenous leg. Amputation and ligation of the artery distal to the aneurysm were performed. He recovered

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The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Department of the Navy or the Naval Service at large.

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and the aneurysm gradually decreased. Bigger reported his experiences with a carotid-jugular arteriovenous fistula of thirty-seven years' duration.[9] He sutured the calcified opening in the artery with interrupted silk. Thirty-two months later an aneurysm developed at the site of repair; an attempt to restore continuity by obliterative aneurysmorrhaphy led to infection and hemorrhage, causing the patient's death. The development of a fusiform aneurysm following repair of artery and vein in a popliteal fistula of twenty-five years' duration has also been recorded.[20] The artery proximal to the fistula was *markedly thinned* and had a diameter of 1.8 cm., whereas the distal artery measured 0.8 cm. A fusiform aneurysm 3 cm. in diameter developed in the repaired artery three months later.

Halsted was keenly interested in the causes of the arterial dilatation in arteriovenous fistulas and aneurysms, and conducted numerous original experiments in an effort to explain these changes.[21] Reid was stimulated to reproduce proximal dilatation experimentally after observing the marked enlargement of the artery supplying the fistula in the patient upon whom he helped Halsted operate. His studies subsequently led him to conclude that proximal dilatation rarely occurred before the first year. The proximal artery became thinner, and contained less elastic tissue.[22, 23] Dilatation in the distal artery may occur if the proximal artery becomes stenosed or occluded from scarring.[20] It is clear, therefore, that the thinning and enlargement of the proximal artery, degenerative changes, and the development of numerous collateral vessels which frequently communicate freely with the arteriovenous aneurysm, are the principal forces which make restorative procedures hazardous in fistulas of many years' duration.

The following case is an example of the development of an aneurysm three years after the repair of a popliteal fistula of fifteen years' duration. It is noteworthy that the collateral circulation was not considered sufficient to ensure a viable foot after this lengthy period of time.

J. P., a 52-year-old man, entered Lane Hospital on Sept. 17, 1945.[25] Fifteen years before this entry to the hospital he was accidentally shot through the left thigh just above the knee. There was a good deal of hemorrhage, requiring ligation of vessels. During the following years "poor circulation" was evident in the leg, the veins dilated, and he developed ulcers on the ankle. Upon examination, pulsation in the left femoral artery was seen, which was twice the size of the right; and a thrill was palpable along it, increasing toward the upper popliteal region. Here a very loud continuous murmur was heard, and compression caused the murmur and thrill to disappear. On Oct. 2, 1945, an arteriovenous fistula, involving the upper portion of the popliteal vessels, was exposed. The artery proximal to the fistula measured 2.5 cm. in diameter and, distal to it, 0.7 cm. The fistula measured 1.5 cm. in length. The accompanying vein was greatly dilated. The walls of the artery and vein had changes suggesting early arteriosclerosis. When the fistula was closed there was no pulsation in the distal artery, and the pedal pulses disappeared, indicating that a repair of the artery was necessary to ensure viability of the foot. A transvenous repair of the arterial opening was performed with arterial silk, using the edges of the vein to imbricate the closure. The vein was ligated. He had an uncomplicated postoperative recovery. In May, 1948, an aneurysm of the popliteal artery, at the site of the previous repair, was noted (Fig. 1, *A*). This gradually increased somewhat in size; and in November, 1948, he was brought to the hospital for a superficial femoral artery ligation. Preliminary to ligation the patient was placed on intermittent compression of the femoral artery below the inguinal ligament. On the third day of this treatment, following twenty minutes of com-

pression, the patient had sudden pain in the left leg, and he noticed that the pulsation in the aneurysm had ceased. The foot became cool, but responded to sympathetic procaine blocks. During the following week he developed a slight fever, which persisted throughout his hospital stay. He was treated with anticoagulants to prevent extension of the thrombosis, and after a few days slight pulsation returned in the aneurysm. At operation on Nov. 18, 1948, a greatly dilated arteriosclerotic superficial femoral artery measuring 3.5 cm. in diameter was exposed (Fig. 1, *B*). The pulsation in the profunda was poor. Due to the size and condition of the artery, ligation was considered to be inadvisable. A left lumbar sympathectomy was performed through a separate, extraperitoneal approach. The aneurysm gradually decreased in size. One year later he had a cerebrovascular accident, which eventually caused his death.

A. *B.*

Fig. 1 (J. P.).—Popliteal arteriovenous fistula of fifteen years' duration, with dilatation of the proximal artery and arteriosclerosis; transvenous repair of the artery. *A*, Popliteal aneurysm appeared three years after repair of artery.

B, Outline drawing of the iliac and femoral arteries to show the persistence of the proximal dilatation three years after the repair of the popliteal fistula.

The thinning and degenerative changes in the proximal artery may not only jeopardize the repair of fistulas of long duration, but may also lead to difficulties with treatment by quadruple ligation. The following case is an illustration of an aneurysm which developed in the altered proximal artery five years after quadruple ligation and excision of a superficial femoral arteriovenous fistula of fifteen years' duration. The collateral blood supply, meanwhile, had regressed somewhat, and it was considered imperative to maintain the continuity of the involved iliofemoral artery. This was accomplished by utilizing the accompanying vein as an inlay in the aneurysm. The vein and the intimal surfaces

of the proximal and distal vessels were united with an inner layer of continuous arterial silk, and reinforced with an interrupted row. This was used in preference to Vitallium tubes, as suggested by Blakemore.[24]

E. C., a 30-year-old man, entered Lane Hospital July 9, 1944. He had been accidentally wounded with a shotgun in the right thigh in 1929. He noticed nothing abnormal until 1931, when a mass appeared. In 1939, he began to have symptoms of heart failure. Upon examination, a pulsating mass was found, with a loud machinery murmur in the right groin. The

A. *B.*

Fig. 2 (E. C.).—*A*, Iliofemoral aneurysm which appeared in the dilated artery proximal to an arteriovenous fistula five years after treatment by quadruple ligation. The fistula had existed for fifteen years.

B, Postoperative view showing the incision employed to expose the aneurysm and inlay the vein graft.

pedal pulses were present. At operation on July 13, 1944,* an arteriovenous fistula of the superficial femoral artery and vein in the upper portion of Hunter's canal was found. The femoral artery proximal to the fistula measured 2 cm. in diameter and was thin, and distal to it measured 0.7 cm. Quadruple ligation and excision were performed. At the end of the procedure the popliteal and pedal pulses were absent. The patient had an uneventful postoperative course, and soon thereafter returned to work. In 1949, approximately five years after the excision of the fistula, while lifting some heavy machines, he noticed

*By Dr. V. Richards and Dr. F. L. Reichert.

the appearance of a swelling in the right inguinal region. This gradually enlarged until September, 1951, when it had reached 8 cm. in diameter. Upon examination this proved to be an aneurysm of the external iliac and common femoral arteries, which had resulted from a rupture of the thin-walled, dilated artery which previously had fed the fistula (Fig. 2). The pedal pulses were present at this time, but disappeared when the aneurysm was compressed. At operation on Oct. 13, 1951, a fusiform aneurysm, measuring 4.3 by 7.8 cm., involving the external iliac and common femoral vessels, was exposed through an

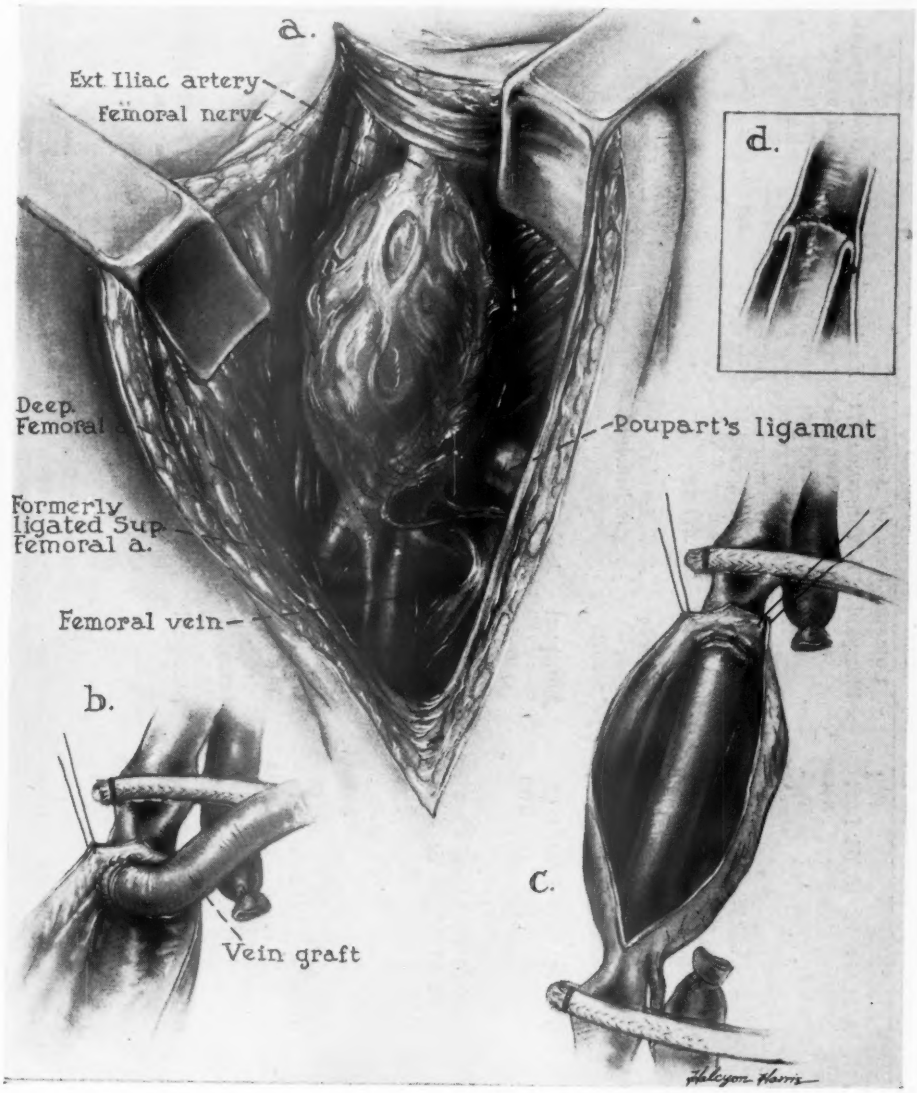

Fig. 3 (E. C.).—Treatment of iliofemoral aneurysm by vein graft inlay, implanted by suture technique. The intima of the vessel leading into and leaving the aneurysm appeared normal. Following the completion of the suture the aneurysm wall was closed over the graft by imbrication.

extraperitoneal approach. The external iliac artery leading to the aneurysm measured 2 cm. in diameter, and the deep femoral artery, distal to the aneurysm, measured 0.8 cm. The superficial femoral artery had become obliterated to the bifurcation of the common femoral. The vessels above and below the aneurysm were dissected, then clamped with arterial forceps. The aneurysm was then opened with a longitudinal incision. It contained a good deal of thrombosis, with a lumen, approximately 1 cm. in diameter, running

TABLE 1. ARTERIOVENOUS FISTULAS AND ARTERIAL ANEURYSMS TREATED BY REPARATIVE PROCEDURES

PATIENT	AGE	RANK	DATE INJURED	DATE OF OPERATION	LOCATION OF INJURY	AGENT	VASCULAR LESION	PROCEDURE	RESULT	REMARKS
						Common Carotid Artery				
A. R.	21	CPL., USMC	9/11/51	12/13/51	Left lower neck	Shrapnel	A-V fistula left common carotid artery and internal jugular vein; lumen 10 mm. in diameter	Excision of fistula, repair of artery and vein	Good function in artery and vein	Asymptomatic
						Brachial Artery				
G. O. H.	28	SGT., USMC	9/29/50	12/11/50	Right arm	Grenade fragments	A-V fistula right brachial artery	Lateral suture of artery, ligation of vein	Viable limb	Normal pulse, associated ulnar and median palsy recovered slowly
G. C.	24	PFC, USMC	9/17/51	12/ 3/51	Right arm	Shrapnel	A-V aneurysm brachial artery and vein	Excision of A-V aneurysm, end-to-end suture of artery, ligation of vein	Normal radial and ulnar pulses	Recovering from partial median nerve palsy
A. McK.	24	CPL., USMC	9/13/51	11/29/51	Left arm	Shrapnel	False aneurysm brachial artery	Excision, 4 cm. vein graft to artery	Normal radial and ulnar pulses	Aneurysm had compressed median nerve-causing partial palsy, which is improving
K. D. C.*	19	PVT., USA	9/19/50	11/13/50	Left groin	Mortar shell fragment	A-V fistula left external iliac A and V; lumen, 12 mm. in diameter	Separation of vessels and lateral suture repair of artery and vein	Normal circulation	Excellent pedal pulses
D. L.	25	PFC, USMC	6/19/51	11/ 6/51	Left groin	Shrapnel	A-V fistula left external iliac A. and V.	Excision of fistula —end-to-end anastomosis of artery	Normal pedal pulses	Right leg amputated overseas after popliteal A. injury; muscular wasting and foot drop from multiple injuries to left leg; preoperative left lumbar sympathectomy

D. W. T.*	22	CPL., USMC	11/ 7/50	12/ 2/50	Upper third left thigh	Bullet	A-V fistula common femoral A. and V., false aneurysm of profunda femoral	Separation of fistula with lateral suture of common femoral vessels, ligation of profunda	Viable limb	Good pedal pulses
C. D.*	19	PFC, USMC	9/17/50	10/30/50	Left mid-thigh	Bullet (50 cal.)	A-V fistula and false aneurysm. Sup. femoral	Excision of fistula and aneurysm—10 cm. vein graft to artery from accompanying vein	Viable limb	Excellent popliteal and pedal pulses
W. C.*	20	HM3 USN	9/23/50	11/10/50	Right thigh	Bullet (50 cal.)	A-V fistula sup. femoral A. and V.	Excision of fistula—7.5 cm. vein graft to artery from accompanying vein	Viable limb	Pedal pulse disappeared on fourth PO day; edema of leg subsided; pulses returned later
S. A. T.*	21	PVT., USMC	10/31/50	12/11/50	Left thigh	Mortar shell fragment	A-V fistula sup. femoral vessels	Excision of fistula—5 cm. vein graft to artery from accompanying vein	Viable limb	Preoperative sympathectomy; excellent pedal pulses; associated sciatic nerve lesion
H. W. U.*	21	CPL., USMC	8/17/50	11/13/50	Right knee	Bullet (25 cal.)	A-V fistula popliteal A. and V.	Transvenous repair of artery, ligation of vein	Viable limb	Preoperative sympathectomy; good pedal pulses; oscillometric index—affected leg 14, left leg 10
E. M.	24	HM3 USN	9/14/51	12/19/51	Right popliteal fossa	Shrapnel	A-V fistula popliteal A. and V., 5 cm. false aneurysm lateral to fistula	Excision of fistula, 7 cm. vein graft from accompanying vein	Viable limb	Preoperative sympathectomy; angiogram shows graft occluded; good pedal pulses from collateral

*Previously reported, West. J. Surg. 59: 625, 1951.

TABLE II. ARTERIOVENOUS FISTULAS AND ARTERIAL ANEURYSMS TREATED BY LIGATION TECHNIQUES

PATIENT	AGE	RANK	DATE INJURED	DATE OF OPERATION	LOCATION OF INJURY	AGENT	VASCULAR LESION	PROCEDURE	RESULT	REMARKS
						Subclavian-Carotid Arteries				
A. C.	21	PFC, USMC	9/16/51	10/19/51	Right lower neck	Shrapnel	Pulsating hematoma from severed right subclavian, laceration of right carotid artery and internal jugular vein	Ligation of right subclavian and carotid arteries and internal jugular vein	Early edema and cyanosis of right hand and arm, which subsided	Complete brachial plexus palsy developed after injury from expanding hematoma
						Axillary Artery				
J. E. L.*	19	PFC, USMC	8/17/50	9/19/50	Right axilla	Mortar shell	False aneurysm second portion axillary artery	Ligation	Viable limb; brachial palsy	Dorsal sympathectomy for coldness and pain in hand
R. H. R.*	22	PVT., USMC	8/18/50	10/10/50	Left axilla and hand	Grenade fragments	A-V fistula with false aneurysm of axillary artery	Ligation	Viable stump	Previous amputation through forearm for severe injuries to hand
C. L. L.*	36	M/SGT., USMC	9/16/50	10/21/50	Left axilla	Mortar shell	A-V fistula and false aneurysm distal third axillary artery	Ligation; ulnar nerve suture	Viable limb	Dorsal sympathectomy for sensitivity to cold; ulnar palsy persists
R. J. S.*	20	PFC, USMC	10/ 2/50	12/20/50	Left axilla	Bullet	False aneurysm distal axillary artery	Ligation	Viable limb	Weak radial pulse; brachial palsy
C. H. W.*	19	PVT., USMC	11/28/50	1/14/51	Left axilla	Grenade fragment	False aneurysm distal axillary artery	Ligation	Viable limb	Brachial palsy from expanding hematoma two weeks after injury
						Brachial Artery				
C. R. F.*	19	PFC, USMC	8/ 8/50	9/ 5/50	Lower third left arm	Bullet	False aneurysm brachial artery	Ligation	Viable limb	Dorsal sympathectomy for sensitivity to cold

J. K.*	21	PVT., USMC	8/17/50	9/21/50	Right arm	Bullet	False aneurysm brachial artery	Ligation	Viable limb	Radial and median nerve palsy resulted from compression of expanding hematoma
C. R. C.*	24	SGT., USMC	9/21/50	11/ 1/50	Left arm	Bullet	A-V fistula brachial artery	Quadruple ligation	Viable limb	
M. E. H.*	18	PFC, USMC	9/17/50		Right arm	Shrapnel	False anuerysm brachial artery	None	Viable limb	Aneurysm thrombosed spontaneously, then slowly regressed
J. B.	22	CPL., USMC	9/11/51	10/19/51	Right arm	Shrapnel	False aneurysm brachial artery distal to profunda	Excision; ligation of artery	Viable limb; reduced radial pulse	Median nerve palsy developed after injury
A. W.	20	FN, USN	7/24/51	9/14/51	Right forearm	Knife	False aneurysm radial artery	Excision; ligation of artery	Reduced radial pulse	Distal end of radial artery pulsated
J. D. W.*	21	SGT., USMC	11/18/50	1/18/51	Upper third left thigh	Bullet	A-V fistula profunda femoral	Quadruple ligation	Viable limb	Preoperative sympathectomy
D. D. G.*	19	PVT., USMC	9/11/50	9/28/50	Right thigh	Mortar shell fragments	False aneurysm sup. femoral artery	Ligation	Viable limb	Sciatic palsy
E. J. S.*	19	PVT., USMC	8/18/50	10/ 2/50	Left leg	Bullet	A-V fistula post-tibial artery	Quadruple ligation	Viable limb	Good dorsalis pedis pulse

*Previously reported, West. J. Surg. 59: 625, 1951.

between the thrombus and the posterior wall. It was obvious that the artery had ruptured anteriorly, producing a false aneurysmal sac. The thrombus was removed, and it was found that the intima of the arteries leading into and away from the aneurysm were normal in appearance. It was decided to implant a segment of the accompanying vein, which was approximately the same size as the normal artery, by direct suture of the ends to the orifices in the sac. Maintenance of arterial continuity in this case was deemed imperative because of the previous ligation of the superficial femoral artery and because of the absence of a distal pulse when the artery proximal to the present aneurysm was clamped. An 8 cm. segment of iliac vein was removed. A continuous intima-to-intima suture with 00000 arterial silk, forming an everted cuff of vein at each end, was done. A second row of reinforcing interrupted sutures was also placed on the cuff. Upon releasing the clamps, the vein distended and the blood flowed freely through the graft. As a support for the vein, the aneurysmal sac was imbricated over the graft with interrupted sutures. The maximum outside diameter of the vein-lined sac then measured 2.3 cm. (Fig. 3). Good pedal pulses could be felt at the end of the procedure. The patient had an uncomplicated recovery. The circulation to the leg is excellent, and to the time of writing, three months later, there had been no local change in the grafted aneurysm.

The difficulties one may encounter in the operative treatment of an arteriovenous fistula of long standing are usually not found in those which have existed for only a few months. Degenerative changes in the involved vessels and marked thinning of the proximal artery have not had time to develop. Although collateral channels have enlarged, they are not of such size or number as to cause the arduous dissections required in old fistulas. These are factors which favor restoration of arterial continuity in fistulas of relatively short duration.

Experiences with the definitive treatment of injuries to the major vessels incurred in both world wars have been documented.[10-12, 26, 27] The present conflict in Korea has afforded an opportunity to treat a number of arteriovenous fistulas and aneurysms of relatively recent origin.* In all, there were twenty-seven patients who had aneurysms or fistulas resulting from instruments of war among approximately 2,000 battle casualties treated in this hospital. It was our intention to restore arterial continuity wherever it proved technically feasible and of possible benefit to the patient. This was true in ten of the twenty-seven instances. All of the extremities remained viable, regardless of the treatment employed, but in a number of instances loss of limb was undoubtedly prevented by arterial repair. Seven of the thirteen extremities which had arterial lesions treated by ligation techniques showed clinical evidence of circulatory impairment. The results of treatment are summarized in Tables I and II.

Of the twelve major arteries which were repaired, ten remained patent as far as could be determined by clinical examination or angiograms. The two failures were in vein grafts. In one instance, a 7.5 cm. graft from the accompanying vein was used to bridge a defect caused by the excision of a superficial femoral arteriovenous fistula (W. C.). Occlusion occurred on the fourth postoperative day, and may have been due to a slight twisting of the graft or to edema. This patient subsequently developed pedal pulses. Another 7 cm. popliteal vein graft thrombosed during the postoperative period, but an excellent collateral had established itself and pedal pulses were present (E. M.). The remaining three grafts were patent during the period of hospitalization: one

*These patients were all hospitalized at the United States Naval Hospital, Oakland, Calif. Nineteen of these cases have been previously reported.[28]

4 cm. brachial (A. McK.), one 5 cm. superficial femoral (S. A. T.) (Fig. 4), and one 10 cm. superficial femoral (C. D.). The last-mentioned case was of special interest since the operation was an emergency procedure for a large, rapidly expanding, false aneurysm associated with an arteriovenous fistula high in Hunter's canal. In spite of the unfavorable local conditions, consisting of considerable edema and extravasated blood, the graft functioned well and probably saved the leg.

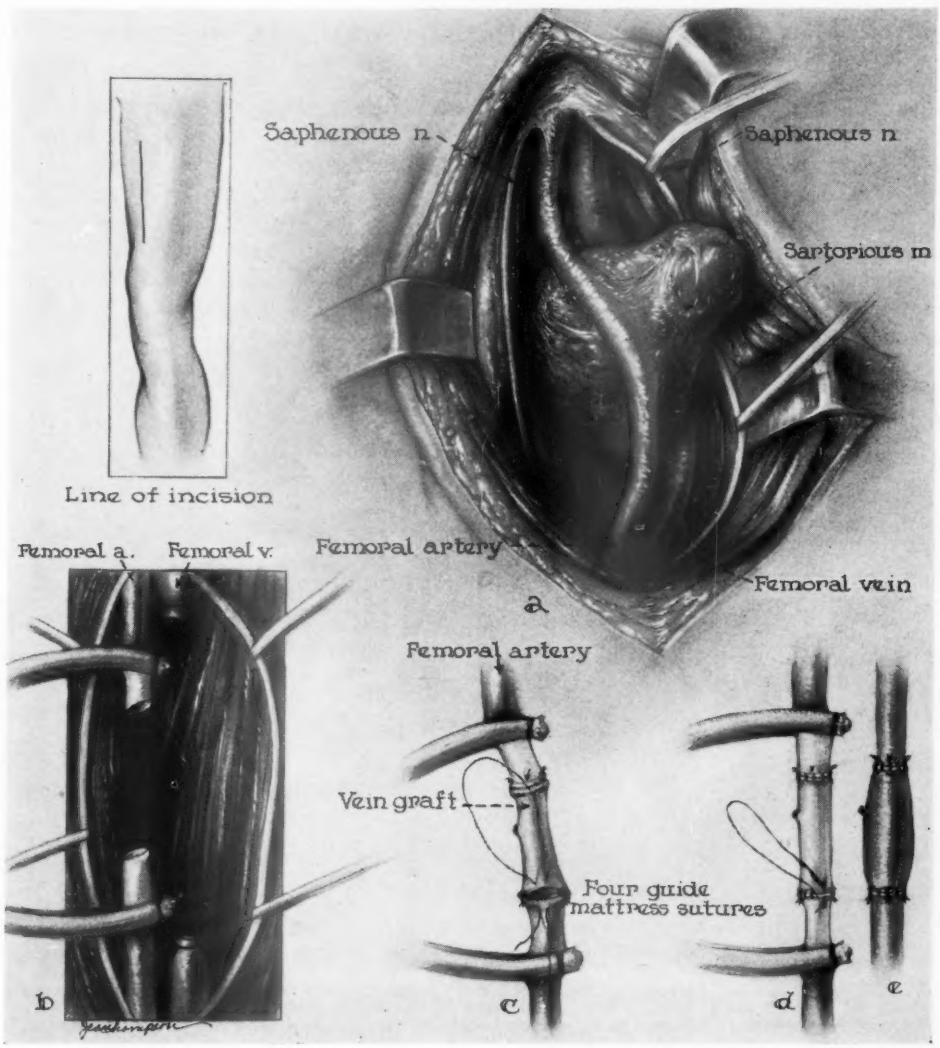

Fig. 4 (S. A. T.).—Superficial femoral arteriovenous aneurysm treated by excision and concomitant vein graft. Four guide mattress sutures are used to prevent rotation and to maintain an accurate fit. The suture is completed with a single continuous layer.

In each of two patients it was possible to separate the artery and vein involved in an arteriovenous fistula in a major vessel. Both fistulas had only a moderate amount of tissue reaction, and it was possible to mobilize them fully. One was a communication between the left external iliac vessels. It was exposed through an extraperitoneal incision, and following suture repair of the separated vessels, a flap of connective tissue was interposed between them. This patient

has normal circulation and returned to duty. The other fistula involved the left common carotid artery and internal jugular vein (Fig. 5). The details of this case are as follows:

A. R., a 21-year-old marine, received shrapnel wounds in the anterior lower neck on Sept. 11, 1951. Subsequent examinations revealed a loud continuous murmur at the base of the neck which was transmitted beneath the sternum. A continuous thrill was palpable

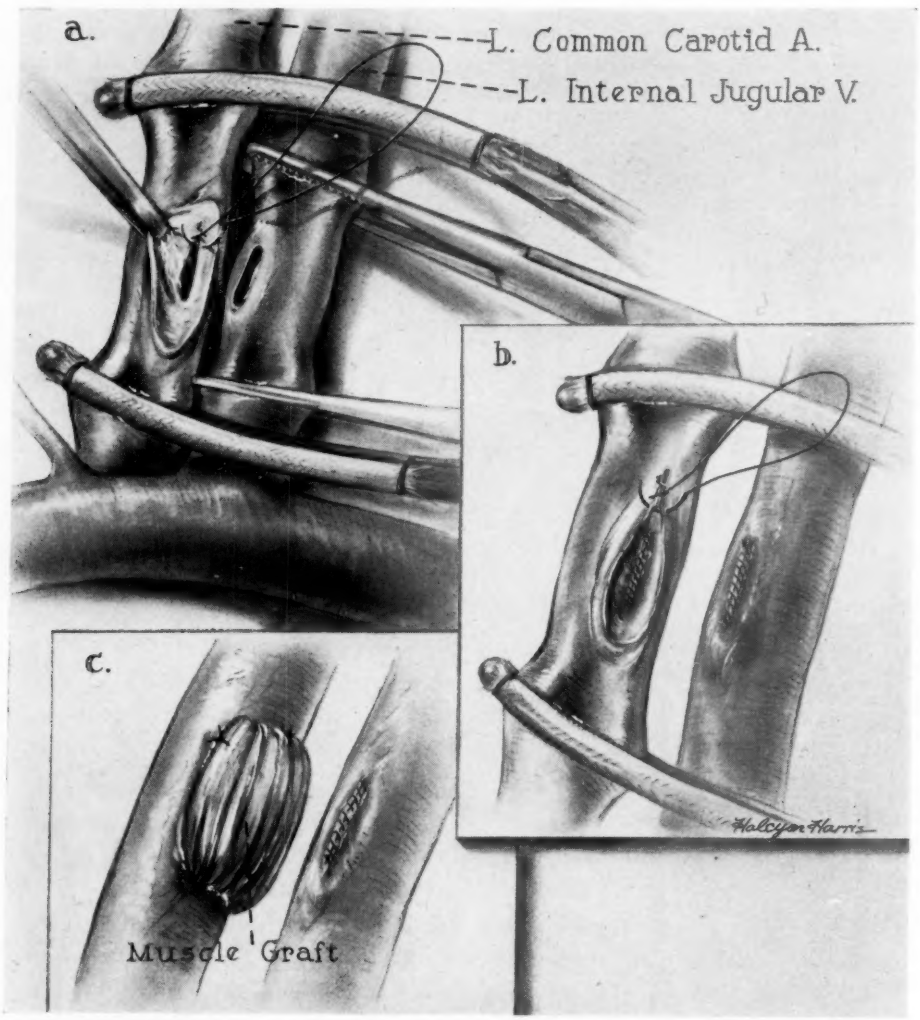

Fig. 5 (A. R.).—Common carotid-internal jugular vein arteriovenous fistula repaired by suture of artery and vein. The remnants of a small aneurysm were used to form a second layer of closure, (*B*) and a free muscle graft was placed over the arterial closure, (*C*).

just above the left clavicle, and it was only with marked pressure that it could be appreciably reduced. It was impossible to determine by examination which vessels were involved. Intermittent digital compression of the left common carotid was practiced for several weeks in preparation for possible ligation. At operation on Dec. 13, 1951, the fistula was approached through an incision over the left clavicle and down the midsternum. A section of the clavicle was removed subperiosteally. An arteriovenous aneurysm of the left common carotid artery and internal jugular vein was found. It was possible to separate the vessels and to repair both, a two-layer closure of the artery being accomplished by suturing a portion of the aneurysm over the repaired opening in the artery. The vein was repaired with a single con-

tinuous suture. A small, free muscle graft was interposed between the two vessels (Fig. 5). The patient had an uncomplicated recovery. Both carotids now pulsate equally, and there is apparently a normal venous return through the jugular vein.

In five instances the involved artery was repaired: twice by lateral suture (G. O. H. and D. W. T.), twice by end-to-end suture (G. C. and D. L.), and once by transvenous suture (H. W. U.). Normal pulses were present during the period of hospitalization in all these cases. In the following patient, the restoration of the iliac artery supplying a badly damaged left leg probably will permit this marine to walk, for an amputation had already been required on the opposite leg.

D. L., a 25-year-old marine, received multiple shrapnel wounds of both legs in June, 1951. A Syme amputation was done on the right foot for gangrene of the toes, resulting from a popliteal artery injury. There were multiple soft tissue wounds in the left leg, a left foot drop, and an arteriovenous fistula of the left external iliac vessels. He was admitted to the base hospital on Aug. 18, 1951, at which time he also had hepatitis and malnutrition. Digital closure of the fistula slowed the pulse from 100 to 80. It was noted that when the fistula was closed, the pedal pulses disappeared, and the foot became cold and numb. Intermittent compression of the fistula was started. In two months his nutritional status was much improved, but there was no apparent increase in the collateral blood supply to the foot, as determined by the effect of obliterating the fistula by compression. A lumbar sympathectomy was performed, and subsequently, on Nov. 6, 1951, the fistula was operated upon. The fistula was excised, the iliac vein was ligated, and an end-to-end anastomosis of the iliac artery was made possible by slight flexion of the thigh. The hip was immobilized in a light plaster cast for two weeks, and normal motion was allowed in three weeks. Good pedal pulses have persisted.

DISCUSSION

In the presence of arteriovenous fistulas of short duration, reconstructive operations designed to maintain and restore normal circulation distal to the fistula are imperative since collateral circulation is minimal. The absence of degenerative changes in the arterial wall makes such restorative procedures feasible and preferable. Another important factor is the age of the patient, which is in effect a measure of the health of his vessels.

On the other hand, in fistulas of long duration, i.e., ten to twenty-five years, marked degenerative arterial changes may be present in the form of calcific deposits at the site of the fistula and arteriosclerosis which militate against effective reconstructive procedures. Occasionally, when such arteries have been repaired, subsequent aneurysmal dilations have occurred at the site of suture. Accordingly, when marked changes are encountered, reconstructive procedures are contraindicated. The abundant collateral circulation in long-standing fistulas permits quadruple ligation in most instances, and this is the operation of choice.

The second pathologic arterial change found in the presence of fistulas of long duration is great dilation of the artery proximal to the fistula. This occurs almost invariably in large fistulas involving the great vessels in the lower extremity, where, in the erect position, gravity as well as lowered resistance at the site of the fistula direct large volumes of of blood through it and back to the heart. The resulting increased flow of blood through the shorter fistulous circuit causes dilation of the artery (and heart) and consequent thinning of the

arterial wall proximal to the fistula. This thinning may be so great as to leave little effective smooth muscle tissue in the wall; and when the fistula is eliminated, the vessel wall cannot contract, the excessively thinned artery remains dilated and under stress may rupture, with the formation of a false aneurysm. Aneurysmal dilation may occur regardless of the operative procedure used to eliminate the fistula, i.e., both quadruple ligation and/or reconstruction of the artery have been followed by aneurysms in this greatly dilated proximal artery. It would be enlightening to know whether prolonged recumbency to avoid the effect of gravity might permit gradual contraction of the dilated proximal artery.

CONCLUSIONS

1. In arteriovenous fistulas of relatively short duration, procedures which restore arterial continuity should be used whenever they are technically feasible.

2. Among a group of twenty-seven arteriovenous fistulas and aneurysms which resulted from instruments of war, it was possible to restore arterial continuity in ten. This was accomplished by separation and preservation of the involved artery and vein in two, repairing the artery in five, and by vein autograft in three. Two other vein grafts became occluded during the postoperative period. All the involved extremities survived, whether treated by ligation or restoration, but seven of the thirteen extremities in which ligation was used showed clinical evidence of circulatory impairment.

3. In arteriovenous fistulas of many years' duration, involving great vessels in the lower extremities, arteriosclerosis and calcification at the site of the fistula make reconstructive procedures hazardous. In addition, great dilation and thinning of the artery supplying such fistulas may result in the formation of an aneurysm proximal to the fistula years after the repair, regardless of whether quadruple ligation or reconstruction of the artery has been employed.

4. An instance of formation of a popliteal aneurysm which followed the repair of a popliteal fistula of fifteen years' duration is described. In another case, an iliofemoral aneurysm followed quadruple ligation and excision of a superficial femoral arteriovenous fistula of fifteen years' duration. A vein graft inlay was sutured into the aneurysm to maintain arterial continuity. Marked dilation and thinning of the proximal artery were present in both these cases, and persisted for years after obliteration of the fistula.

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DISCUSSION

DR. MICHAEL E. DE BAKEY.—I had hoped that others would discuss this very interesting paper. I think it would be regrettable to let it go without emphasizing some of the points that Dr. Gerbode has made. First, I would like to say that I was interested, particularly, in the incidence in which they found arterial lesions in the 2,000 battle casualties. It is a little higher than the general incidence found in World War II, but, of course, a series so small may have statistical aberrations. It does, however, come within the range of order that one might expect, that is, anywhere from 1 to 3 per cent. The particular observation that I think is worthy of thoughtful study concerns the patient who has an arteriovenous fistula of long duration. We have had occasion to observe several patients who had arteriovenous fistulas for as long as twenty-five to thirty years or more, a few of whom have been admitted with heart failure, probably on the basis of the fistula. In such cases we have noticed this particular dilation, thinning, and sclerosis of the proximal artery and it has made the problem of adequate repair a hazardous procedure. It is our belief, however, that every effort should be made to try to maintain continuity of the arterial

channel for two reasons. First, because it is important to obtain as good circulation as possible in the peripheral vascular bed in these old people and second, because they are already beginning to develop arteriosclerotic changes and circulatory deficiency. Therefore, maintenance of blood flow in the main arterial channel to get as much flow of blood to the distal part as possible is highly desirable and, in that respect, it is preferable to quadruple ligation and excision.

DR. A. H. BLAKEMORE.—Dr. Gerbode has presented some important aspects of surgery of major blood vessels.

Certainly the now common practice of successful restitution of arterial blood flow by anastomosis following excision of traumatic arteriovenous fistula of the major extremity vessels constitutes an important advance in surgery in the direction of complete rehabilitation of the patient. The above plan of surgical management is usually feasible in cases operated upon within six months to a year following injury. Or, in younger patients, success may be achieved even after longer periods following injury.

In cases of long-standing arteriovenous fistulas, particularly in the older age group, quadruple ligation with excision of the fistula remains the procedure of choice, and it can be depended upon to cure the patient.

As is well known to most of you, there is the occasional neglected patient having an arteriovenous shunt of long standing who may be in a critical condition from circulatory failure. Such cases require special handling and judgment in the selection of a surgical procedure that will not overburden the patient but will ameliorate the strain. I refer to such procedures as complete ligation of the vein proximal to the fistula with varying degrees of occlusion of the artery proximal to the fistula. For example, some two years ago I felt compelled to do such a palliative procedure in a 54-year-old man who was in cardiac failure from a large arteriovenous fistula of the femoral vessels of some twenty years' duration. Operating under local anesthesia, I placed rubber bands wrapped with Polythene film containing the tissue irritant dicetyl-phosphate around both femoral vessels just proximal to the fistula. The band upon the vein was secured by a mattress suture of silk to the point of complete occlusion, whereas the artery was closed down almost to the point of disappearance of the palpable thrill.

DR. MARK M. RAVITCH.—Dr. Gerbode mentioned the interest of Dr. Halsted and Dr. Reid in these problems. Just a few days ago, there was discharged from the surgical service a patient now in her fifties, who was a child of seven years when she was operated upon by Dr. Halsted and, a few years later, by Dr. Reid, with Dr. Halsted looking over his shoulder. The difficulties which they had with her emphasize the difference in the character of the congenital arteriovenous fistulas and the acquired, traumatic arteriovenous fistulas. Dr. Halsted performed a long and difficult operation (her fistula was in the neck), separating and dissecting out the carotid artery through an enormous incision and laying back the parotid. Incidentally, both his incision and Dr. Reid's have healed beautifully and, despite the extensive dissection, she never had a facial palsy or any other difficulty. They ligated many arteries and veins, excised large venous sacs. Gradually, the mass recurred and actually new veins appeared. Dr. Reid reoperated and found new vessels and new connections and excised those and, although the condition has now remained static for almost forty years, she still has, as was demonstrated by clinical examination and by arteriography, arteriovenous communications, demonstrating the fact that these communications in the congenital fistulas are frequently multiple. And, as you know, more particularly in the extremity, but occasionally high in the neck, the fistulas may involve vessels within the bone marrow so that in the extremities we are sometimes forced ultimately to amputation in order to effect a cure and, in the neck, sometimes are forced to attempt a resection of the mandible in an effort to bring about a cure.

THROMBOENDARTERECTOMY FOR ARTERIOSCLEROTIC THROMBOSIS OF MAJOR ARTERIES

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THE feasibility of thromboendarterectomy to restore the patency of major arteries occluded by arteriosclerosis has been studied at the University of California Hospital in a series of 26 patients. Previous reports by Dos Santos and others have indicated that in selected cases of arterial thrombosis due to arteriosclerosis it is possible to resect the diseased interior of thrombosed arteries and to reconstruct these arteries by suturing the remaining outer coat of media and adventitia.[1-6] It has been the experience of these surgeons that when occlusion is limited to a segment of a major artery, thromboendarterectomy will in many cases restore the peripheral arterial circulation. Such operations have been applied to the arterial tree from the abdominal aorta to the popliteal arteries. Studies in the Experimental Surgical Labortory of the University of California School of Medicine have demonstrated the process of intimal regeneration following excision of the internal lining of the aorta of dogs.[7] The use of fascia lata to strengthen the walls of arteries following thromboendarterectomy in animals and in three of the first six patients upon whom this operation was used has been described. It is the purpose of this report to describe the subsequent experiences in the application of thromboendarterectomy to the problem of arteriosclerotic arterial occlusion. Over a one-year period, 83 patients with peripheral arteriosclerotic vascular disease were examined. In 26 of these patients, coexisting conditions, such as severe coronary artery, cerebrovascular or renal disease, or advanced age, contraindicated any major surgical procedure. Arteriographic studies were not performed on any of these patients.

Of the 57 remaining patients with arteriosclerotic arterial occlusion, arteriography was performed in 52. Arteriograms were not made in 5 cases in which thrombosis involved only the smaller arteries of the lower leg, inasmuch as it appears probable that thromboendarterectomy is not technically feasible in vessels of small caliber. Of the 52 patients with occlusion in the major arteries proximal to the popliteal artery who were studied by arteriography, 14 were believed to be unsuitable for operation because of extension of thrombosis distal to the popliteal artery (Fig. 1), or because of the additional presence of advanced thrombosis in the smaller arteries of the lower leg. Arteriography demonstrated thrombosis involving principally a segment of the arterial tree proximal to the popliteal artery in 38 patients. In a few cases, the distal arteries were not satisfactorily visualized. Decision for operation in these cases was based upon the possibility of improving the circulation by the removal of a localized obstruction which could be visualized in a major artery. Thromboendarterectomy was refused by 1 patient, attempted but abandoned in 4, com-

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pleted in 26, and is pending in 7. Of the 4 cases in which the operation was not completed, 2 showed such extensive periarterial inflammation that accurate dissection could not be performed. In the other 2, the marked thickening of the wall of the distal patent arterial segment made it impossible to find an uninvolved area in which to start the intimal excision.

Operative techniques (Figs. 2 and 3) similar to those described by dos Santos, Leriche, and Bazy were applied in all cases. Continuous spinal anesthesia was used. Exposure of the aorta and its abdominal branches was obtained through a long, midline, transperitoneal approach, transecting the pubic attachments of the rectus abdominis muscles if necessary to expose the external

Fig. 1.—Femoral arteriogram of a patient with arteriosclerotic thrombosis of the superficial femoral artery. The failure of the popliteal artery to fill with Diodrast from the collateral arteries indicates that thrombosis has extended beyond the level amenable to thromboendarterectomy.

iliac arteries. The femoral artery was exposed by an incision paralleling the course of this artery. For exposure of the popliteal artery, the tendinous attachment of the adductor magnus was divided. After the thrombosed artery was freed from the adjacent tissue, a bloodless field was obtained by occluding the artery proximally and distally with rubber tubing or special clamps. Branching vessels were temporarily occluded in a similar manner. A single long incision was used to incise the adventitia and media of the thrombosed segment of artery. The incision was extended beyond the occluded segment distally to a zone of minimal thickening of the arterial wall. A plane of dis-

section was developed by incising circumferentially the arterial intima in this zone of minimal intimal thickening distal to the thrombosed segment. Proximal dissection in the plane between the intima and media was used to remove the thrombosed and often calcified interior of the occluded artery. A similar technique was used in 3 cases in which the artery was not completely occluded. A continuous over-and-over suture of 00000 Deknatel silk through all layers was

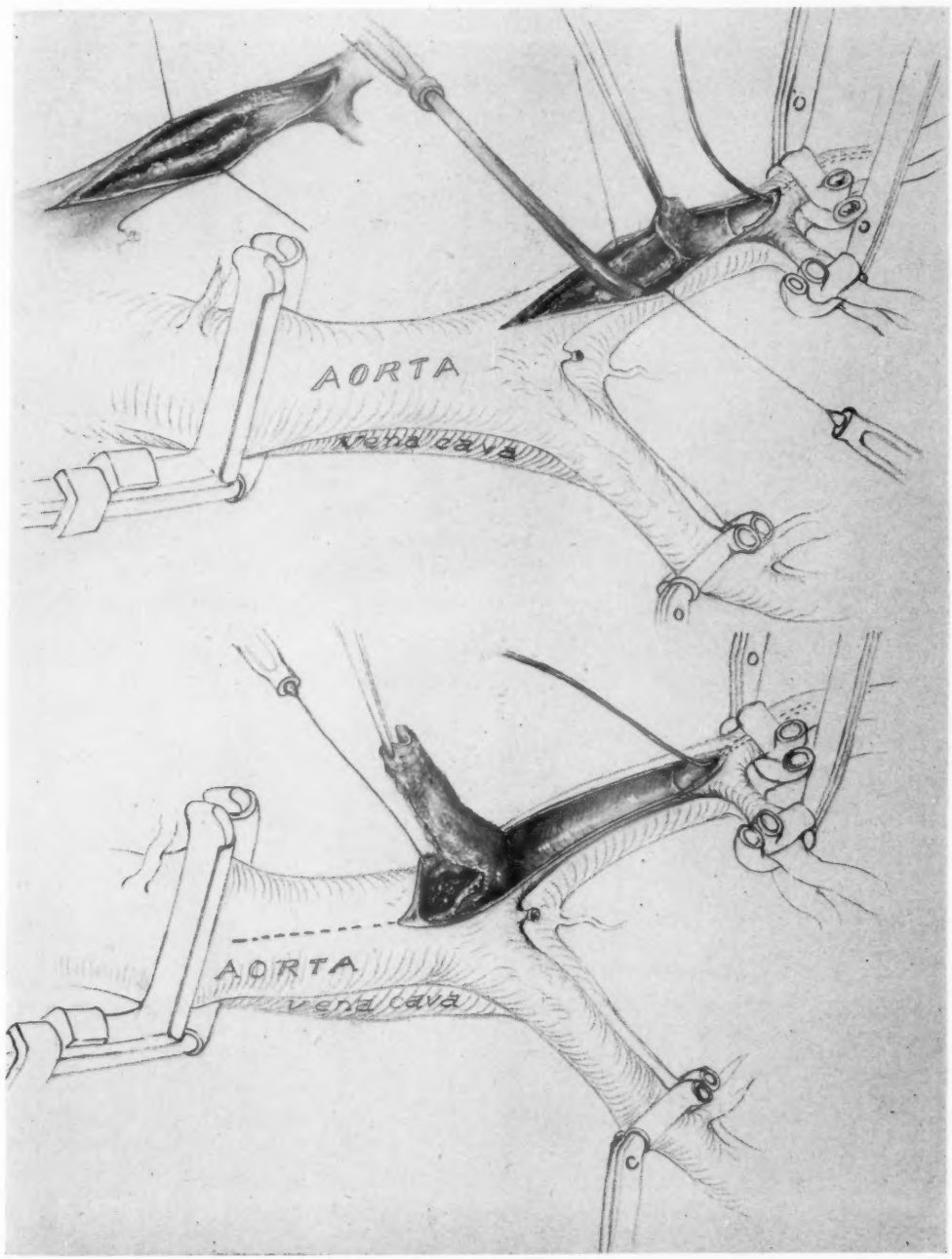

Fig. 2.—Operative technique for thromboendarterectomy in a patient with thrombosis of the left common iliac artery. (Aortograms in Fig. 4.)

used to close the arterial incision. In 5 of the operations, an additional supporting layer of fascia lata was used. Heparin solution in a concentration of 100 mg. per liter of 5 per cent glucose in water was used to irrigate the arterial lumen during closure. For the purpose of minimizing the tendency to thrombosis in the arteries distal to the occluding clamps during the period of operation, heparin in similar concentrations was injected continuously at a rate of 1 c.c. per minute through a Polythene tube passed through the distal occluding

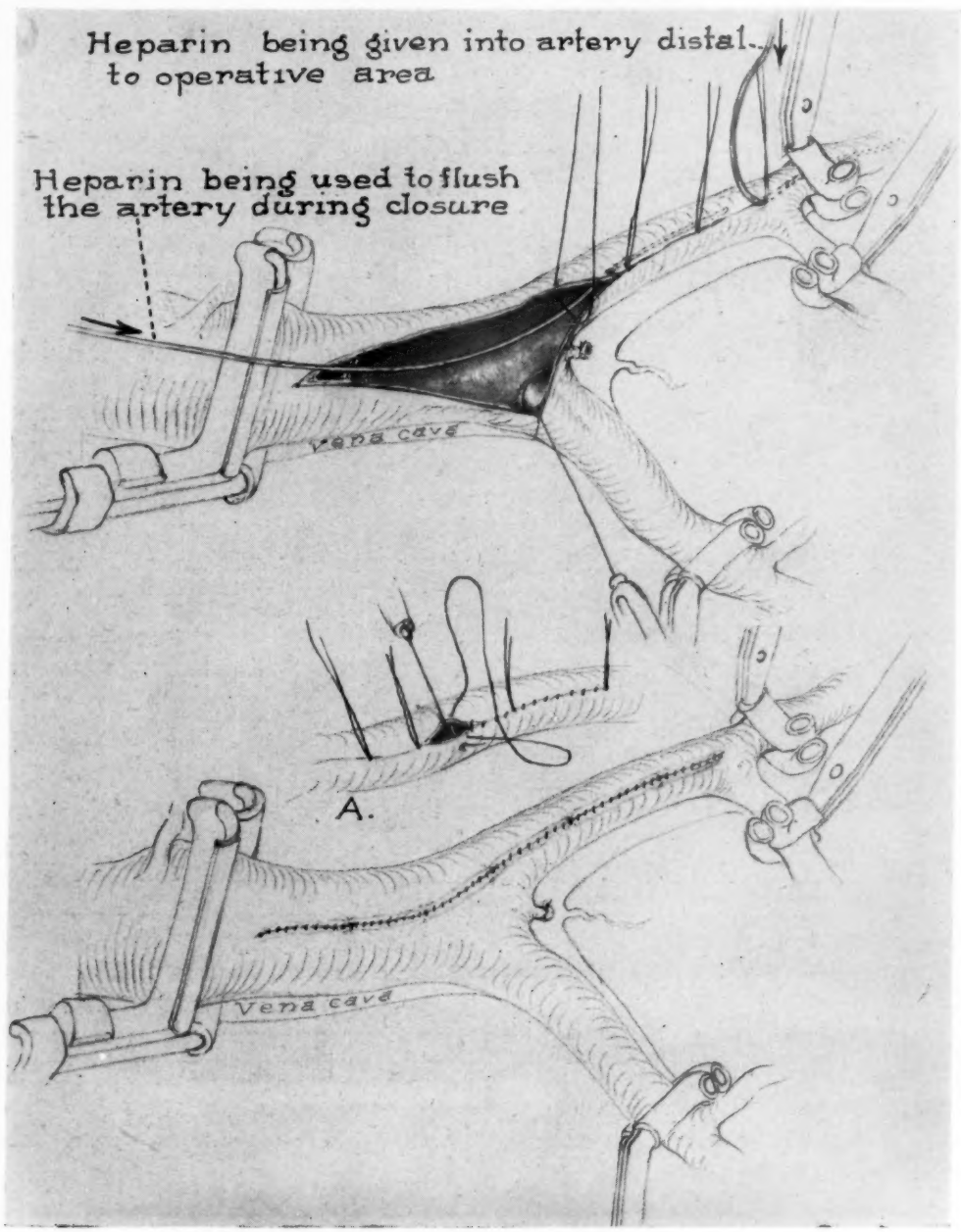
Heparin being given into artery distal to operative area
Heparin being used to flush the artery during closure
Vena cava
A.
Vena cava

Fig. 3.—Method of closure of the remaining arterial wall.

clamp into the lumen of the artery distal to the operative area. This tube was removed after the arterial incision was closed. Heparin in similar solution was then given intravenously at a rate sufficient to maintain the clotting time between 20 and 25 minutes. A rate of 1 to 2 c.c. per minute was usually necessary for this purpose. In most of the patients, heparin was given in this manner for 48 hours and then discontinued. No other anticoagulant therapy was used. In 4 patients, no heparin was given after operation.

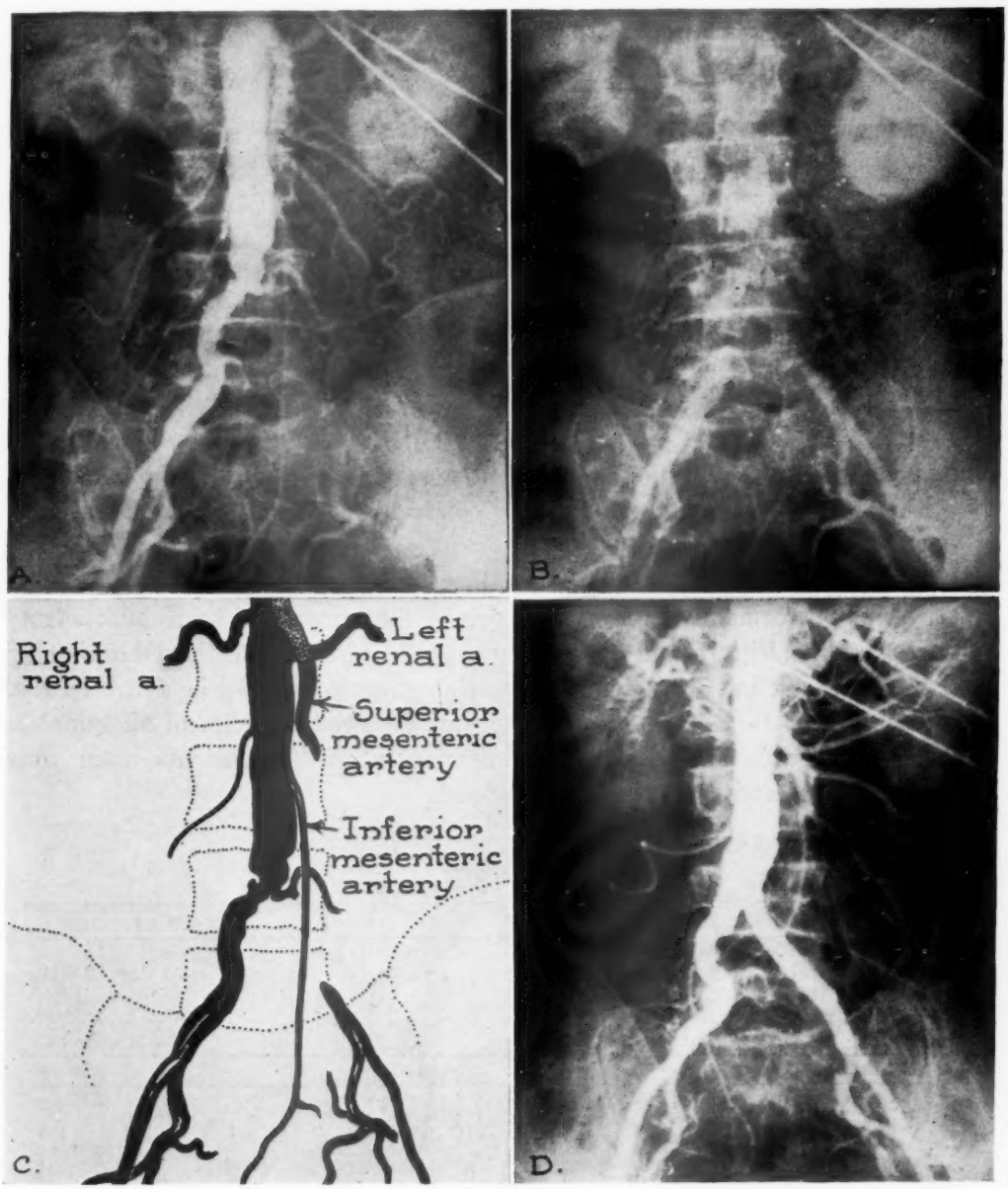

Fig. 4.—Preoperative (*A* and *B*) and postoperative (*D*) aortograms demonstrating thrombosis of the left common iliac artery and stenosis of the right common iliac artery. The aortogram *B* was taken 5 seconds after the aortogram *A* to demonstrate the distal level of occlusion. The artist's drawing (*C*) is a composite of *A* and *B*.

The level and extent of thrombosis in the patients upon whom thromboendarterectomy has been performed and the length of the resected specimens are indicated in the following table:

TABLE I

LOCATION OF THROMBOSIS	NUMBER OF CASES	AVERAGE LENGTH OF OCCLUSION (IN CM.)	AVERAGE LENGTH OF SPECIMEN (IN CM.)
Aorta and iliac	5	14	17
Aorta, iliac, and femoral	1	31	52
Iliac	5	6	12
Iliac and femoral	2	22	26
Femoral	10	12	25
Aorta and iliac (incomplete occlusion)	3		
Total	26		

The number of patients with thromboses involving the aorta and iliac arteries was relatively larger in the operative series than in the entire series of patients examined. This may indicate that arteriosclerotic thrombosis involving the aorta or iliac arteries has a greater tendency to persist as a localized process than thrombosis involving the femoral artery. In all cases the length of intima resected was greater than the length of the total occlusion. In several patients with thrombosis of one common iliac artery, the other common iliac artery was observed to be partially occluded by arteriosclerotic thickening of the intima. In such cases, thromboendarterectomy was performed in both arteries (Fig. 4). In 3 patients, resection of the intima of the aorta or iliac arteries was performed where only stenosis of the lumen had been demonstrated by aortography (Figs. 5 and 6). The symptoms of complete thrombosis at this level were present but weak femoral arterial pulsations could be felt. In these 3 patients, restoration of a normal lumen was followed by relief of all symptoms of ischemia. Table II indicates the outcome in the 26 patients upon whom thromboendarterectomy has been performed.

TABLE II

OPERATIVE RESULTS			NUMBER OF CASES
Peripheral circulation restored			15
Peripheral circulation improved			4
Peripheral circulation unchanged			1
Amputations performed			3
Died			3
Total			26
Lumen at operative area patent			25
Pedal pulsations restored		18	
Pedal pulsations not restored		7	
Distal thrombosis present before operation	4		
Distal thrombosis occurred during or after operation	3		
Lumen at operative area occluded			1
Total			26

The longest follow-up period has been 13 months (Fig. 7). Fourteen patients have been followed for over 6 months after thromboendarterectomy. Observations on the circulatory status of all patients following operations have included oscillometry, skin temperature studies, and arteriography whenever possible. The arterial lumen at the site of operation has remained patent in 25 patients. In the patients who died or on whom subsequent amputation was necessary, thrombosis had not developed in the operative area. The patient whose circulation is recorded in Table II as "unchanged" is the only one in whom thrombosis occurred in the operative area. In this case, thrombosis

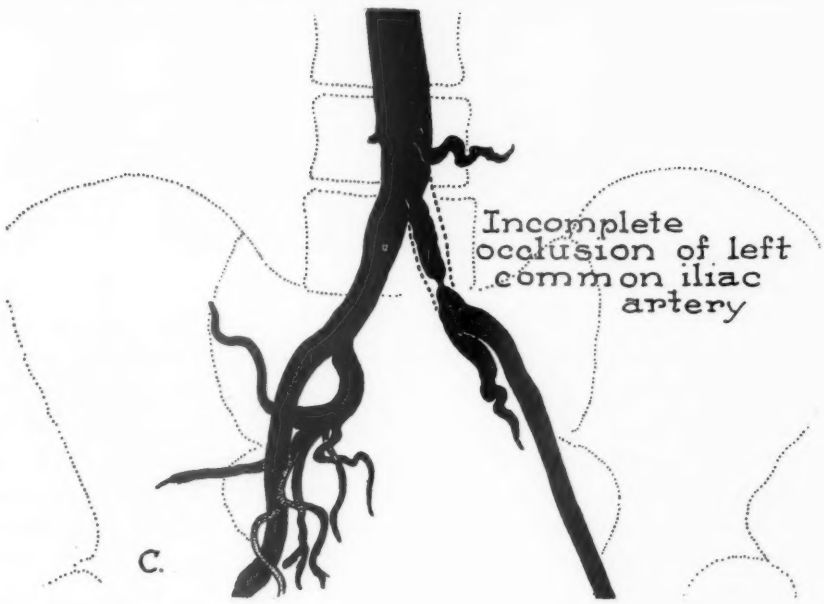

Fig. 5, *A*, *B*, and *C*.—Aortograms demonstrating stenosis of the left common iliac artery before and after operation. Following thromboendarterectomy, claudication and muscular atrophy disappeared.

developed immediately after thromboendarterectomy was performed for a segmental occlusion of the femoral artery. At the time of operation on this patient, it was observed that the wall of the popliteal artery distal to the thrombosed segment was unusually thickened by the arteriosclerotic process. Fifteen patients were studied by arteriography four weeks after thromboendarterectomy. Unusual arterial dilatation in the operative area was observed in only one (Fig. 8). In the 15 patients whose symptoms were completely relieved, pedal arterial pulsations have been palpable since operation (Fig. 10).

Fig. 6.—Specimen removed at operation (Fig. 5) showing the diaphragm-like plaque partially occluding the arterial lumen.

The preoperative symptoms in this group included claudication in all, rest pain in 5, and sexual impotence in 5, the last occurring in men with occlusions at the level of the aorta or iliac arteries. In most of these patients, atrophy of the thigh or calf muscles was present before operation. Following operation, muscle tone and volume slowly returned to normal. In 2 patients with gangrenous areas on the foot, rapid healing of the necrotic areas took place following thromboendarterectomy. In the 4 cases in which the circulation is recorded as "improved," severe rest pain had existed before operation. This was relieved in all; the peripheral skin temperature and sensation returned to normal, but mild claudication persisted. In two of these, arteriography before opera-

tion had demonstrated thrombosed segments separate from the operative area and involving the arterial tree distal to the popliteal artery. In the other two, thrombosis distal to the operative area developed during or immediately after operation (Fig. 11).

Amputation was performed on 3 patients who developed peripheral gangrene. One patient had a gangrenous toe secondary to thrombosis of the femoral artery before operation. The failure to salvage the extremity after successful thromboendarterectomy was attributed to multiple thrombosis of arteries in the

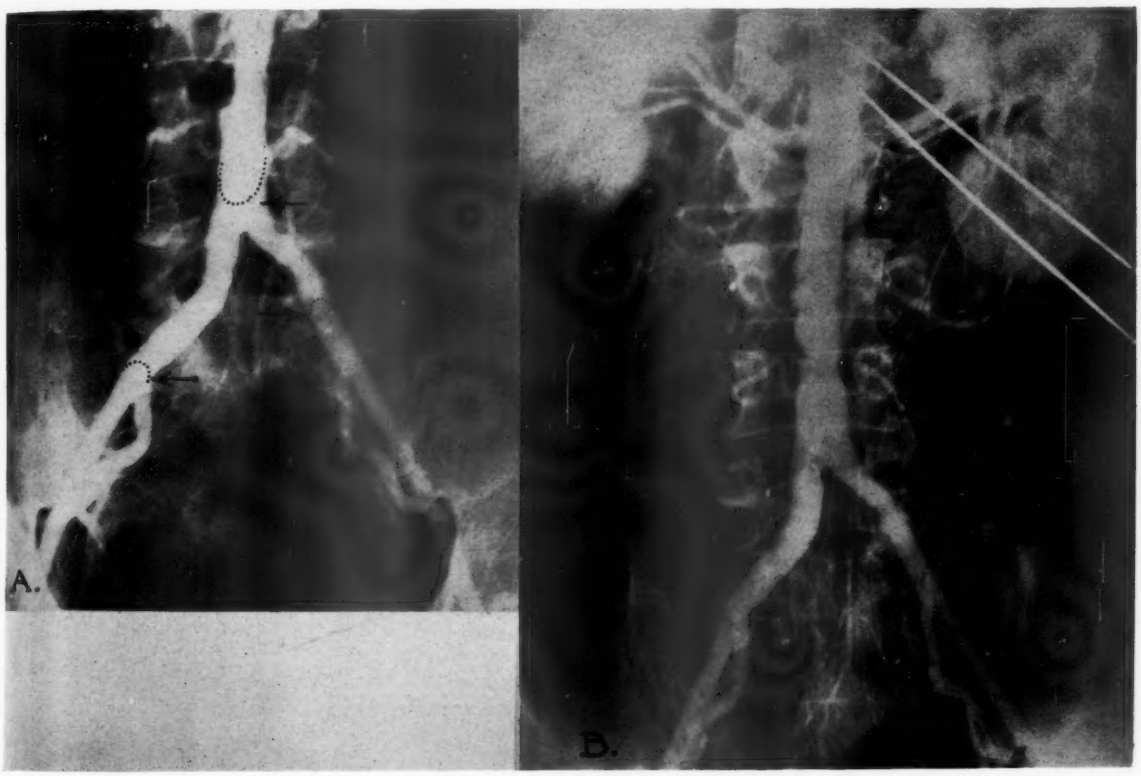

Fig. 7.—Aortograms at 1 month (*A*) and 13 months (*B*) following thromboendarterectomy for arteriosclerotic thrombosis of the abdominal aorta and common iliac arteries. The arrows in *A* indicate the proximal and distal levels of complete occlusion before operation. The operative findings have been illustrated in a previous report.[7]

lower leg, determined by arteriography of the resected extremity. A second patient was operated upon for acute iliac artery thrombosis of 16 hours' duration. Popliteal pulsation appeared and the zone of demarcation descended from the upper thigh to the ankle but the tissue beyond this level had developed irreversible ischemic necrosis. In a third patient, necrosis of the wall in the operative segment of a femoral artery was followed by rupture on the fourteenth postoperative day. Hemorrhage was controlled by ligation of the artery but subsequent gangrene of the lower leg required amputation.

Three patients died in the immediate postoperative period, one from retroperitoneal hemorrhage, and two from cerebrovascular thrombosis occurring at 9 and 20 days, respectively.

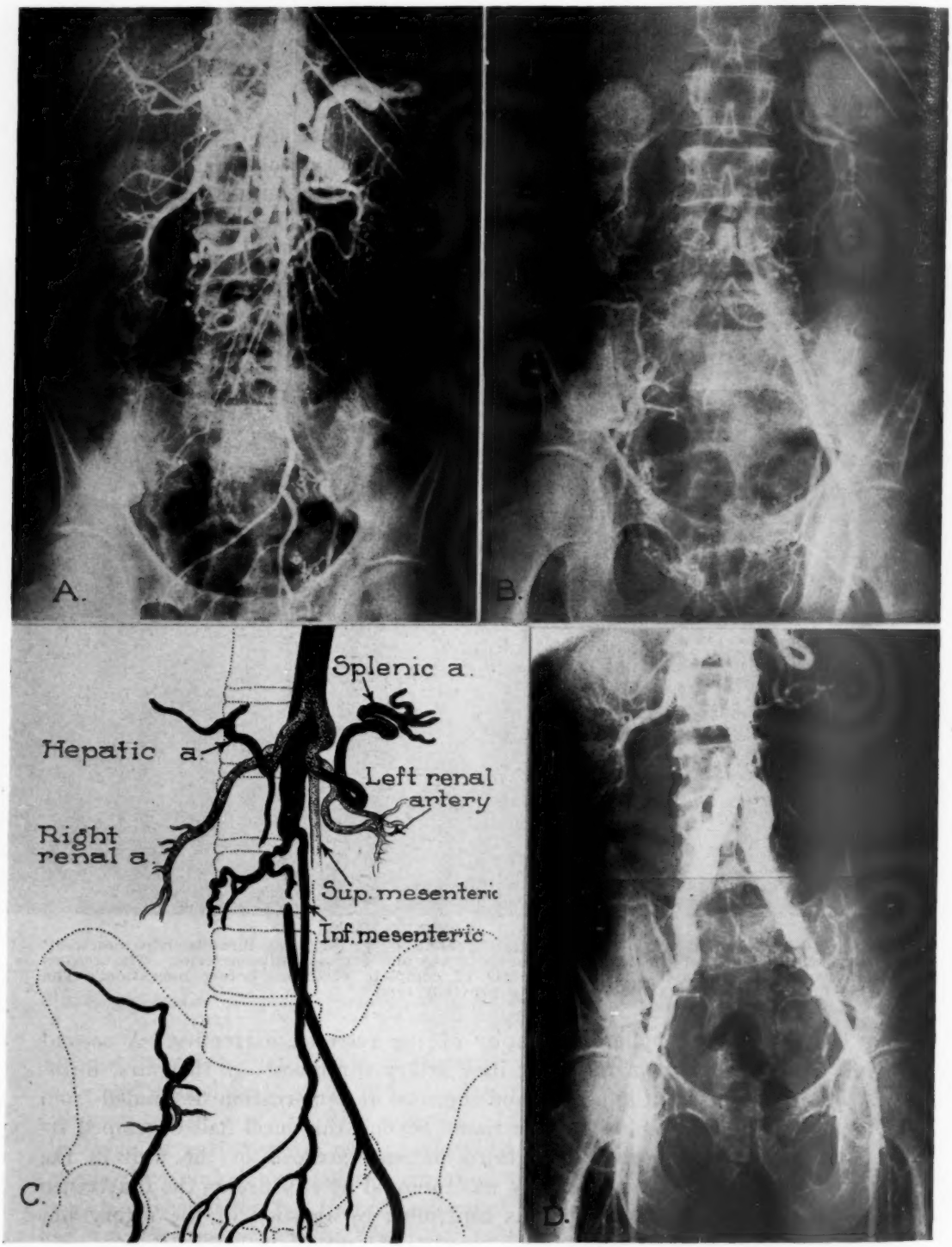

Fig. 8.—Aortograms demonstrating thrombosis of the aorta and both common iliac arteries. At operation an aneurysm of the aorta proximal to the level of occlusion was discovered. The intima was resected to a level proximal to the aneurysm. This portion of the aorta was reinforced with a layer of fascia lata after closure of the media and adventitia. Slight dilatation of the iliac arteries can be observed in the postoperative aortogram (*D*).

Hemorrhage following operation occurred in only 3 cases. In the patient whose femoral artery ruptured due to local necrosis, heparin had been discontinued 12 days before. In the patient whose death from retroperitoneal hemorrhage is recorded above no obvious source of the bleeding was observed at postmortem examination. In a third patient, diffuse wound bleeding developed 36 hours after operation. The coagulation time was found to be in excess of 60 minutes. Bleeding ceased after the administration of 100 mg. of protamine, which lowered the coagulation time to 20 minutes.

Fig. 9.—Specimen removed at operation in the case illustrated in Fig. 8, showing the aneurysm of the aorta.

Measurements of peripheral skin temperature before and after operation were taken at basal conditions with the patients exposed in a room at 20° C. The average temperature of the toes before operation under such conditions was 21° C., the temperature usually found in a person with normal arterial circulation. In most of the patients whose arterial pedal pulses were restored, basal skin temperatures rose to 27° C. to 30° C. for a period of 5 to 7 days and

Fig. 10.—Right femoral arteriogram in the patient with thrombosis of the aorta and iliac arteries illustrated in Fig. 8, demonstrating the patency of the peripheral arterial tree.

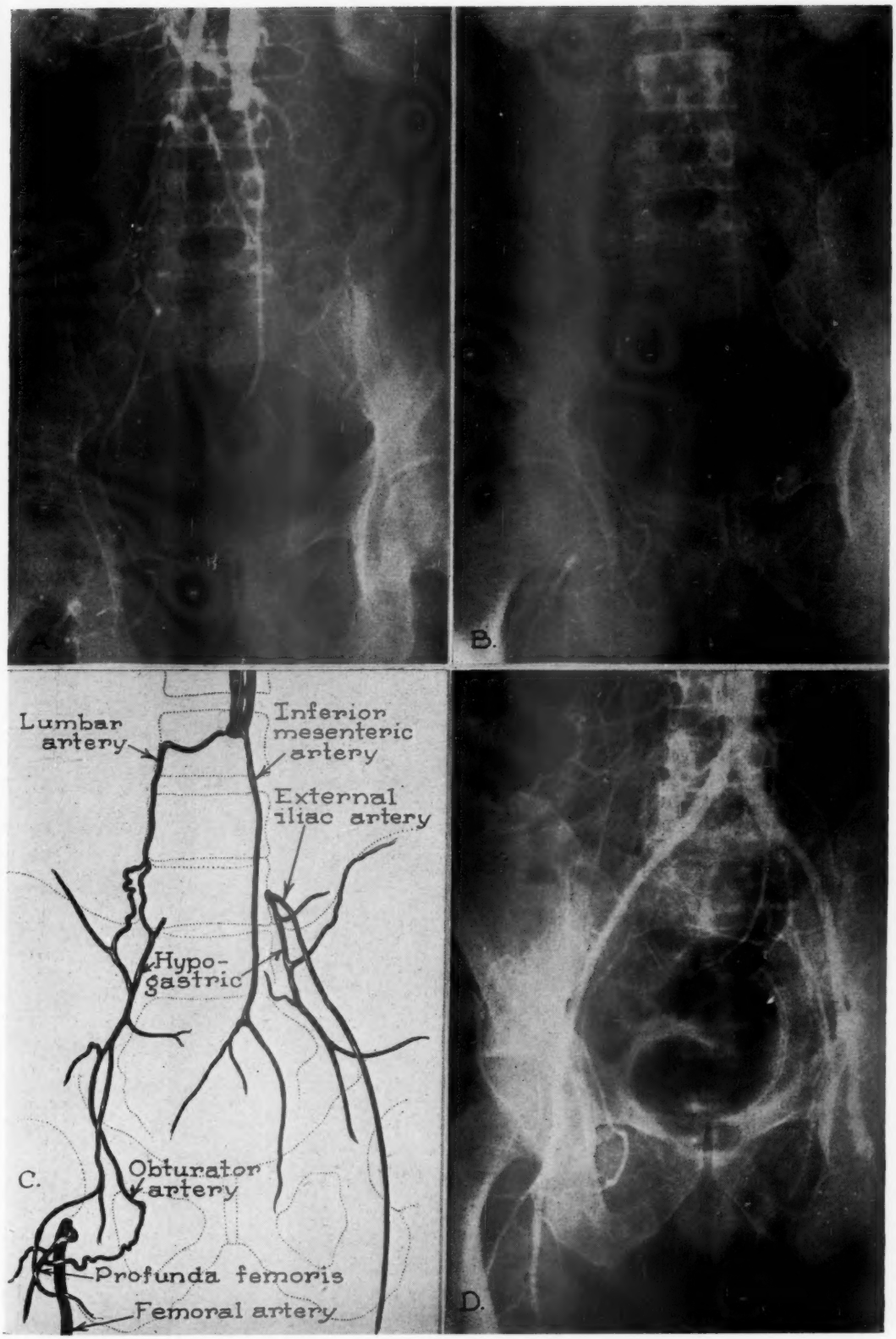

Fig. 11.—Aortograms demonstrating thrombosis of the terminal aorta and the iliac and common femoral arteries bilaterally. Although this patient's symptoms were improved following operation, the postoperative aortogram (*D*) demonstrates thrombosis of the superficial femoral arteries distal to the operative area which was observed clinically within an hour after operation.

Fig. 12.—Aortograms demonstrating stenosis of both common iliac arteries due to arteriosclerosis, before (*A*) and after (*C*) thromboendarterectomy. In the interval between the preoperative aortogram and the operation, intraluminal thrombosis distal to the stenotic area on the left caused complete occlusion of the left common iliac artery.

then slowly returned to normal. It is believed that this transient rise in peripheral temperature is due to the interruption of periarterial sympathetic nerve fibers. Vasodilatation tests were performed by a modification of the Landis and Gibbon method. Preoperatively, in most cases, heat applied to the trunk produced either no elevation, or less than normal elevation of the temperature of the lower extremity. A complete rise in skin temperature (10° to 12° C.) by reflex vasodilatation was the usual finding after successful thromboendarterectomy. In 6 patients, lumbar sympathectomies had been performed previously. Four of these failed to show a rise in peripheral skin temperature until after thromboendarterectomy had been performed. Skin temperatures were then maintained at a level of 31° to 32° C.

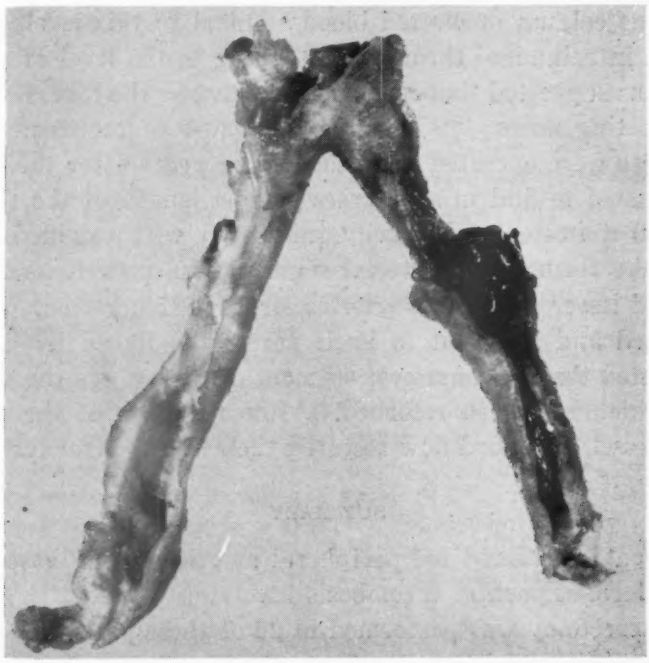

Fig. 13.—Specimen removed at operation in the case illustrated in Fig. 12. Note the intraluminal thrombus on the left, which has progressed to the level of the bifurcation of the common iliac artery.

During the course of this study, observations have been made concerning the mechanism of arterial thrombosis in arteriosclerosis. Thickening of the arterial wall in a localized area by arteriosclerotic changes in the intima sufficient in degree to cause peripheral ischemia has been observed in 3 patients. In two of these, fresh thrombi, adherent to the wall of the artery for a short distance distal to the zone of narrowing, were found at operation. Two other patients were observed over a period when a similar type of localized stenosis in one common iliac artery progressed to complete obliteration of the arterial lumen before operation (Fig. 12). In both cases, the clinical history indicated an episode of sudden peripheral ischemia at the moment of total occlusion. At operation the lumen of the artery distal to the level of stenosis was occupied by

a fresh blood clot which extended in one to the bifurcation of the common iliac artery (Fig. 13) and in the other to the bifurcation of the common femoral artery. The arteriographic studies on most patients in this series showed occlusions ending proximally and distally at the level of major arterial branches. These findings have suggested that at the moment of complete occlusion by the primary arteriosclerotic process the static column of blood proximal and distal to the level of original occlusion clots, and that the progression of such a clot may be arrested by the flow of blood at the level of collateral arteries. A different mechanism of occlusion was observed in two patients who were operated upon within a few hours of the onset of symptoms. Incision of the outer wall of the artery in these cases revealed the interval between the media and intima to be filled with freshly clotted blood. The intima at this level was collapsed in the center of the column of clotted blood. Distal to this level, the lumen was occluded by an intraluminal thrombus extending to the level of a large arterial branch. This has suggested that hemorrhage between the layers of an artery, as is seen in dissecting aneurysms, may be the cause of occlusion in some cases. Most of the cases were operated upon months or years after the onset of symptoms. It was usual to find in such cases a short length of the thrombosed segment of normal diameter and heavily infiltrated with calcified material. The remainder of the thrombosed arterial segment was usually smaller and, upon incision, showed lesser degrees of arteriosclerotic degeneration. The intima was usually collapsed and adherent to itself across the lumen by fibrinous bands. This has suggested that the narrower segment of artery was the site of an intraluminal clot which had been resorbed. After resection of the intima and resuture of the vessel, the blood flow restored the arterial diameter to normal.

SUMMARY

Of 83 patients examined for peripheral arteriosclerotic vascular disease 38 were found to have segmental thrombosis involving principally a major artery. Thromboendarterectomy was performed in 26 of these patients. Patency of the previously occluded arterial segment was successfully restored in 25. The peripheral arterial circulation was restored or improved in 19. The operative technique of thromboendarterectomy used in these cases and the method of anticoagulant therapy following operation are described. Observations made during this study on the mechanisms of arterial thrombosis in arteriosclerosis are discussed.

ADDENDUM

Since the time of preparation of this manuscript, thromboendarterectomy has been performed on 12 additional patients. In 10 of these, patency of the previously thrombosed aorta and common iliac arteries has been successfully restored. One patient died from rupture of the aorta suture line 28 days after operation. One patient with occlusion of the femoral artery developed an obstructing thrombus in the operative area immediately after operation. In the last 4 patients upon whom thromboendarterectomy was performed for occlusion of the aorta or iliac arteries, no anticoagulant therapy was used in the postoperative period.

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DISCUSSION

DR. T. HIERTONN.—Mr. Chairman and members of the Society: In accord with this very interesting paper of Dr. Wylie, I should like to report on a similar case of the Leriche syndrome which Prof. Clarence Crafoord and I treated in the same way last year. The method is very well described by Dr. Wylie and our case perhaps will show some different points about the history. It was in June last year that a 31-year-old man was referred to our Orthopedic Outpatient Department. According to his physician, the patient was suffering from tired back, pain in the thigh and knees. The only objective symptom was a poorly developed weak back. There were no neurological signs. The patient was thus introduced as a case of lumbago sciatica, having done heavy work for years and having been perfectly well until December, 1950, when he sought medical care for backache. He was treated with local injections. Immediately after treatment, he sensed some stiffness in the back, but gradually his back grew better. He continued to work through January and February, 1951, but he was stopped by pains in the iliac crests and internal aspects of the thighs, especially in connection with heavy work. Later, his left leg began to feel numb and very weak. The condition grew progressively worse during the spring of 1951, and the patient's own description of his symptoms from that period is typical of intermittent claudication. When I made the first examination in the Outpatient Department, the pulsations were found to be much weaker in the left groin than the right. The same difference was noted at the level of the knees; neither the dorsal artery on the foot nor the posterior artery were palpated. The patient appeared to be in good general condition, the Wassermann test was negative, and the sedimentation rate was 2 mm. an hour. Oscillometer readings on the left side were considerably less pronounced than on the right. The exercise oscillogram, according to Aaron, showed a delayed reverse reaction of several minutes before the operation. Aortography by Dr. Lindblom showed a large, uneven narrowing at the bifurcation. The picture was interpreted as a thrombus astride the bifurcation extending down in both common iliac arteries leaving a very narrow lumen on both sides. It was somewhat larger on the right than on the left side. The diagnosis was either tumor compressing the arteries from without or an obstruction within the lumen. Under expectant treatment during the summer months, the patient's condition deteriorated to the point that he was no longer able to work. It was clear that something had to be done to try to check the arterial circulatory disturbance which had progressed steadily for 6 or 7 months and, finally, incapacitated the patient. Clarence Crafoord, who was consultant, conceded that exploration was indicated, stating in his preoperative opinion, that "chimney sweeping" or removal of the obstruction according to the method of Dos Santos was required but that it might also be necessary to remove the pathologic area. If the latter step was taken, it would be necessary to insert a graft to restore the circulation. The operation was, therefore, postponed until a suitable graft could be procured. At operation, he succeeded in removing the obstruction according to the

method we have seen described by Dr. Wylie. After suturing the artery, we had rather good patency. This is a case of early Leriche syndrome and I will only stress the importance of aortogram in such cases.

DR. WARREN COLE.—I would like to commend Dr. Wylie and others on the work they are doing because I think it will distinctly decrease the incidence of arteriosclerotic gangrene in certain patients, if we choose the right patients. My remarks are really based largely on the work of Dr. Julian, working in our clinic. He has operated on about 25 patients with arteriosclerotic obstruction in the iliac or femoral arteries and has deviated slightly from the method that Dr. Wylie has presented insofar as he has excised the obstructed portion of the artery and inserted a vein graft in each of about twelve of them Obviously, the vein graft should be done on those having a long segment of vessel occluded by the sclerotic process. In the ones having a short obstructed segment, the local removal of the plaque with end-to-end anastomosis will be adequate. In these patients that Dr. Julian has operated upon, performing a vein graft, he has been able to achieve a pulse in either the dorsalis pedis or posterior tibial in at least several of them. I remember one man in particular who before operation could walk only one-quarter of a block because of claudication. When seen several weeks after operation, which consisted of excision of an obstructed segment with vein graft, he was able to walk two miles. If we get a few patients like that I think it will be distinctly encouraging to carry on this work, perhaps choosing the cases very carefully, hoping that we can prevent severe changes later on.

DR. WYLIE (Closing).—I wish to thank the discussers for their comments regarding their experiences with this problem. I believe that Dr. Hiertonn's case is particularly significant. We have encountered several patients with complete or partial occlusion of the aorta or iliac arteries who, because of the localization of their pain to the low back, hips, or thighs, were initially treated for possible orthopedic disorders.

We have been interested in the possibility of using vein grafts to replace thrombosed segments of major arteries but have observed in experimental animals that endarterectomy is technically less difficult than vein grafting. In most instances of arteriosclerotic thrombosis, major arteries branch from the occluded arterial segment, or just distal to it. Since these branches are frequently patent, removal of the thrombus from the parent artery restores arterial flow into the branching arteries. Resection of the diseased segment of artery and restoration of continuity by the use of a vein graft would in many instances mean the sacrifice of these collateral vessels. The advisability of providing an intact endothelium by the use of a vein graft may be more theoretical than real in view of the low incidence of postoperative thrombosis which we have observed after thromboendarterectomy.

AUTOTRANSPLANTATION OF THYROID TISSUE IN THE TREATMENT OF LINGUAL THYROID

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LINGUAL thyroid, while uncommon, is not rare. In 1942, Bajkay[1] presented a review of 267 probable cases of this disease, and in the ten-year period, 1936 to 1945, Goetsch[2] found 14 cases reported.

A congenital lesion, more common in female than in male children, origin from an embryologic rest of the anlage of the thyroid gland at the base of the tongue is the generally accepted explanation of the anomaly. It is interesting that the lesion does not occur within the muscular portion of the tongue, but that invariably at least a portion of the tumor is submucosal.[3] Although additional thyroid gland may be present in the neck, the lingual tumor represented the only thyroid tissue present in the body in about 70 per cent of the reported cases. Since the parathyroid glands have a different embryologic origin, these structures are not involved in the anomaly, and bear no adjacent relationship to the tumor.

The significance of the disease depends primarily on mechanical factors due to the position and size of the tumor. In its typical location just beneath the mucosa at the base of the tongue between the epiglottis and the circumvallate papillae, the degree of interference in swallowing, phonation, and respiration will depend primarily on size. Symptomatology may be totally lacking, and the tumor is found in routine examination, or because of sore throat or tonsillectomy. This is more often true in the child before puberty. The tumor, however, in later life may reach the size of an orange. Hemorrhage from surface erosion is an occasional symptom. In addition, the lingual thyroid is heir to all the pathologic ills which may derange the normal gland. Hypo- or hyperthyroidism occasionally occurs, and even carcinoma has been reported.[4]

The differential diagnosis includes other tumors or cysts which may occur in this area. Of some value in this regard is the use of tracer doses of radioactive iodine (I^{131}).[5, 6] This technique also has the advantage of demonstrating the presence or absence of thyroid tissue in the normal position in the neck.

The use of radioiodine in therapeutic doses, as has been suggested,[7] appears to us irrational. This treatment, if effective, should inevitably lead to marked athyroidism, whether or not normal thyroid tissue were present in the neck. This was apparently the result in the reported case.[7]

The indication for surgical removal rests on the presence or incipient threat of unpleasant or dangerous symptomatology. Dysphasia may lead to tracheal aspiration; dysphonia may be quite annoying; or dyspnea may limit

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work capacity. A symptomless mass of fair size in a 10-year-old child may prove to be the cause of obstruction at onset of puberty. Heretofore, the surgical attempt has been either total or subtotal excision via either a transoral or a suprahyoid approach. However, a frequent and serious sequela is profound hypothyroidism.[8-12] At least three cases are on record in which transplantation of the tissue was attempted, but in all cases failure was apparently experienced in the take of the graft.[13-15] If such a technique could be devised, surgical excision followed by transplantation would be the logical therapy for this interesting anomaly.

This paper reports our clinical and experimental experience in the attempt to elaborate a successful technique for autotransplantation of thyroid.

CASE REPORT

L. B., a 9-year-old Spanish-American girl, was first admitted to the Colorado General Hospital on July 5, 1949, because of a mass at the base of her tongue. This mass had been first noted six months earlier when her mother examined the patient because of a sore throat. There had been no previous symptoms referable to this region. The mass persisted after the sore throat subsided, and the patient was referred to this hospital.

The firm, purplish red mass, located at the base of the tongue in the midline, measured about 2 cm. in diameter. Otherwise, physical examination and laboratory data were normal. On July 9, 1949, the lesion was excised by a transoral approach. It was encapsulated, and came out easily. At the operating table the tumor was sectioned and recognized as thyroid tissue. While frozen section was being obtained, the neck was palpated and explored through a tracheostomy incision. No thyroid gland was felt in the normal position. Frozen section confirmed the diagnosis of normal thyroid tissue. The gland was then divided into three pieces. One was transplanted to the right pectoralis muscle, one to the right rectus abdominus muscle, while the third section was stored in Ringer's solution containing 10 per cent human plasma and kept refrigerated at 4° C. The postoperative course was uneventful. Basal metabolism rate obtained prior to discharge was +15; weight was 66 pounds.

Two months later she was admitted for radioiodine studies and basal metabolism determinations. In the interval, she had noted an increased appetite and had gained 12 pounds. The basal metabolic rate was –17 and there was no uptake of the tracer. The stored portion of the patient's lingual thyroid was then transp'anted to the liver.

Following the second admission she was put on thyroid extract, one-half grain daily, because of weight gain, sluggishness, and dryness of the skin. This was discontinued a month before her third admission which was on December 7, 1949, five months after the first operation. The basal metabolic rate was –28, blood cholesterol 220 and she weighed 84 pounds. Radioiodine tracer studies again failed to show any uptake of the tracer.

Because the patient was definitely in a state of hypothyroidism it was felt worth while to try a homograft. Accordingly, she was admitted for the fourth time on Dec. 28, 1949. The superior portion of a thyroid lobe taken from a patient with Graves' disease was transplanted with arterial anastomosis to the external carotid artery on the right.

During the next two months, the patient became more alert and her mother said she thought her hair had become finer though the patient took thyroid extract for only one week in the middle of this period. On her fifth admission on Feb. 23, 1950, her basal metabolic rate was –19, blood cholesterol was 200 mg. per cent and she weighed 84 pounds. Radioiodine studies showed an uptake of the tracer for the first time. The activity was in the two areas of initial autotransplantation though it was less than 5 per cent. There was no activity in the neck.

The patient remained alert and the skin moist and fine without medication until the next admission on April 3, 1950, when tracer studies showed a 20 per cent uptake by the

autografts in the pectoralis and rectus muscles. Her weight was 88 pounds, basal metabolism rate –20, and blood cholesterol 218 mg. per cent. She appeared to be in a state of low euthyroidism.

The radioiodine studies were repeated on Sept. 29, 1950, again with 20 per cent uptake. Weight on this, the seventh admission, was 103 pounds, basal metabolic rate –27, and blood cholesterol 189 mg. per cent. Because the patient was apparently entering menarche and because of the weight gain she was placed on one-half grain of thyroid extract daily.

During the next year she felt well and was alert and active. On Oct. 22, 1951, her blood cholesterol was 173 mg. per cent, basal metabolic rate –12 and weight 105 pounds. Radioiodine uptake at this time was only 5 per cent, but she had been off thyroid extract for only two weeks. She was, therefore, kept off supplemental extract until Dec. 28, 1951, when tracer studies were repeated. The uptake at this time was 21 per cent and was still limited to the areas of autotransplantation done at the time of the excision of the lingual thyroid.

DISCUSSION

Faced at the operating table with the realization of having removed all of this young girl's thyroid gland, we had no experience or knowledge of how to proceed. The desirability of autotransplantation was obvious. How best to do it? What shape the pieces, how big, and into what sites?

The two sections of the gland immediately transplanted were approximate thirds of the globular tumor, and measured at least .5 cm. in their least dimension. The third segment was preserved as we were then storing our arterial homografts in plasma-Ringer's solution at 4° C. The thought was that if Hal-

TABLE I. SUMMARY TABLE OF PERTINENT DATA IN CLINICAL PATIENT

DATE	TREATMENT	B.M.R.	WEIGHT (POUNDS)	I^{131} UPTAKE (PER CENT)
July, 1949	Lingual thyroidectomy, autotransplants to pectoral & rectus muscles	+15	66	
September, 1949	Stored autotransplant to liver	–17	75	0
December, 1949	Homotransplant to neck	–28	84	0
April, 1950	None	–20	88	20
October, 1950	Thyroid extract, one grain daily	–27	103	20
October, 1951	Taken off thyroid	–12	105	5
December, 1951	Resume thyroid, one grain daily		111	20

sted's[16] theory concerning autotransplantation of parathyroid were true of thyroid, then we might have a better chance for take after hypothyroidism had developed. She did become athyroid, and two months later this segment was placed into liver, thinking that a very vascular site might be desirable. At the time of transplant, however, the tissue did not appear to be viable.

Five months after the original removal and transplantation, the patient was in a profound hypothyroid state. A homograft with direct arterial anastomosis of the superior thyroid artery of a hyperplastic donor lobe to the external carotid of the patient was tried without too much enthusiasm. The net result of this maneuver was a cervical hematoma, as there was no venous outlet for the graft.

In the next few months, however, the patient's clinical condition showed progressive improvement. Nine months after the initial autotransplantation radioiodine studies, previously negative, for the first time revealed a significant

(20 per cent) uptake, and monitoring showed all the activity to lie in the muscular autografts. It was apparent that the tissue had taken and survived, but that there had been a six- to nine-month lag before hormonal output had been resumed.

When the patient began to show the body changes of puberty and entered menarche, the level of thyroid hormone output from her transplants, which had been sufficient to maintain her in a low euthyroid state. appeared to be no longer adequate. Supplemental thyroid extract was needed. Could it be that the thyroid graft did not respond to pituitary stimulation? Tracer studies were then performed, first after a short withdrawal from thyroid medication and a

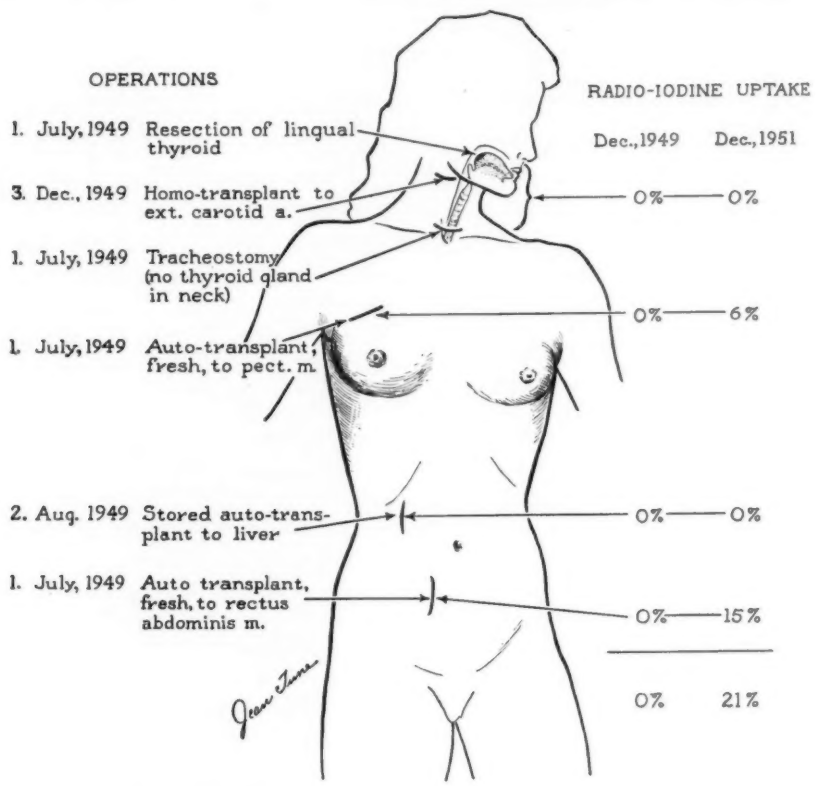
OPERATIONS
RADIO-IODINE UPTAKE
Dec., 1949
Dec., 1951
1. July, 1949 Resection of lingual thyroid
3. Dec., 1949 Homo-transplant to ext. carotid a.
0% 0%
1. July, 1949 Tracheostomy (no thyroid gland in neck)
0% 6%
1. July, 1949 Auto-transplant, fresh, to pect. m.
2. Aug. 1949 Stored auto-transplant to liver
0% 0%
1. July, 1949 Auto transplant, fresh, to rectus abdominis m.
0% 15%
0% 21%

Fig. 1.—Diagrammatic representation of operative procedures and radioiodine studies of the thyroid grafts.

two-week period of iodine-free diet. The uptake was only 5 per cent. Two months later, after more prolonged abstinence from medication and a two-week period of iodine-free diet, the uptake rose to the previous level of 21 per cent. These studies are interpreted as follows: Thyroid extract by mouth suppressed the thyroid stimulating hormone of the pituitary so that hormone output from the grafts was diminished. Withdrawal of medication released the pituitary stimulus with resultant increase in transplant activity. The grafts are under hormone control, but are not large enough to supply adequate hormone in periods of stress, although they do suffice for average growth and vital requirements.

EXPERIMENTAL STUDIES

To answer the operative difficulties posed by this patient, the problem was taken to the experimental laboratory. Various shapes, sizes, and sites for thyroid autotransplantation in dogs were evaluated.

It was early observed microscopically that segments of any size showed degenerative changes in the center while the cells on the periphery retained their architectural integrity. This strongly suggested that a large surface area was desirable. Accordingly, the technique was adopted of first removing all of the capsule and then cutting the gland to be transplanted into thin slices, 1 to 2 mm. thick (similar in shape to a slice of bread), transferring the multiple pieces into a trough or cut in the recipient tissue. This method resulted in apparently complete survival of all cells. Other dimensions besides thickness do not appear to be important.

Transplantation sites chosen for study varied in regard to vascularity, and in addition were limited to practical clinical areas. Anterior chamber of the eye, therefore, was not used. Liver and spleen suggested themselves as providing a maximum blood bath and fatty subcutaneous tissue as essentially avascular, muscle being intermediate. A series of six animals was observed. Interestingly enough, sites appeared to be unimportant in the survival rate of grafts when the thin-slice technique was used. All such grafts survived, regardless of the recipient tissue. Theoretically, since liver is known to destroy thyroxin, this site would be undesirable. Since muscle or subcutaneous tissue are equally adequate and much more easily available these appear to be the sites of choice.

The experimental transplants were studied with tracer doses of radioiodine. No activity was noted at 4 months, although microscopically the tissue appeared normal. Apparently the lag between survival and function noted in the clinical case is a constant phenomenon.

As a result of these studies, therefore, we would recommend the following technique for autotransplantation of thyroid: The capsule should be carefully dissected from the gland, which should then be sliced into sections 1 to 2 mm. in thickness. These should be transferred into troughs in muscle or subcutaneous tissue in at least two separate sites, lest initial infection or subsequent injury destroy all the grafts.

SUMMARY

1. In a 9-year-old girl, removal of a lingual thyroid was recognized as total thyroidectomy. Three types of thyroid transplantation were attempted: immediate autograft to muscle, delayed autograft to liver, and homograft with arterial anastomosis.

2. Only the immediate autografts to two muscular sites survived two years later.

3. There was a six- to nine-month lag before the surviving grafts showed hormonal activity as determined by clinical evidence and radioiodine tracer studies.

4. The autografts appear to be under hormonal regulation by the pituitary gland.

5. Experimental studies in the dog suggest that a successful and practical method for autotransplantation of thyroid is to remove the capsule, slice the tissue into thin pieces 1 to 2 mm. in thickness, and bury the segments in either muscle or subcutaneous tissue.

6. Hypothyroidism at the time of transplant (Halsted's "demand by the body for the hormone") is not a prerequisite for successful grafting of thyroid.

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DISCUSSION

DR. EDGAR J. POTH.—I should like to ask a question of Dr. Swan. Might there not be some danger of doing damage to the few remaining, functioning thyroid cells in these transplants with even small tracer doses of radioactive iodine? The concentration of the iodine could be such as to give a lethal dose of irradiation to the functionally active thyroid tissue.

DR. SWAN (Closing).—I think the point is an extremely good one. We were very nervous about what the dosage size of our tracer should be, so we began by using very small doses—in the neighborhood of 5 μc. Then, when we did not get any result, we worked it up. In this April one, we were using a 200 μc dose. When we had the uptake we were quite worried that we might have hurt the small transplants by giving that much of a dose. I think the answer comes down to the dose compared to the grams of tissue involved. Our radiologist felt that, in very small level tracer doses, this would not deposit a sufficient amount of radioiodine to jeopardize the survival of the grafts. It certainly is an important point, and I agree it might be injurious.

THE RETENTION OF CERTAIN PLASMA VOLUME EXPANDERS WITHIN THE CIRCULATION OF HUMAN SUBJECTS FOLLOWING A 1,000 CUBIC CENTIMETER HEMORRHAGE

A Preliminary Report

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THE problem of selecting the one best plasma expander among those now available is proving to be a difficult one. Some are being eliminated on the basis of demonstrable toxicity but the remainder must be judged on the basis of comparative efficacy. Animal experiments are of some value in that more or less standardized shock can be established and the expanders compared on the basis of their influence on survival rate and blood pressure response. In the last analysis, however, it is essential to know of what value these agents are in human subjects and preferably in those in need of transfusion. Unfortunately patients in shock or those undergoing major surgery do not constitute a sufficiently uniform group in which to compare agents, most of which are very nearly equal in their effects.

A number of substances have already enjoyed rather extensive clinical trial and the number of expanders available is being steadily increased especially as the manufacturers are able to supply the same substances in a variety of forms by varying the particle size. Since all of these substances must be compared eventually in human beings it has seemed important to us to try to establish a standardized procedure which could be carried out by any investigative team with a reasonable hope of comparable results. In the interest of uniformity of subjects, it seemed best to use healthy young male subjects who were free of disease. Second, it seemed worth while to conduct the experiments under conditions in which the blood volume was in need of expansion. Preliminary hemorrhage of approximately 1,000 c.c. is safe and while this introduces some variability into the experiments it can be achieved over a fairly uniform bleeding period and the volume can be adjusted somewhat according to the subject's body size. We have accepted this variable rather than collect data on unbled subjects in whom an expander would be expected to maintain a supernormal blood volume. Third, it seemed important to control rigidly fluid intake and activity of the subjects, all of whom were therefore hospitalized for 24 hours on the metabolic ward of the University Hospital.

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There seemed to be two available approaches by which comparative efficacy could be judged in humans. If analytic methods are available to quantitate the expander, it is possible to follow its fate in the body as to intravascular retention and urinary excretion. Thus, ideally, an expander should remain in the blood stream until native plasma protein can replace it, after which it should completely disappear from the body. The second approach is to follow blood volume over a period of time after hemorrhage and infusion with the expectation that a good expander will maintain a fairly uniform blood volume. Since red cells have been lost, the plasma volume should be maintained above normal until new red cells are produced.

It has been shown by Ebert, Stead, and Gibson[1] and by others[2] that in subjects comparable to ours who are bled 1,000 c.c. but given no replacement, spontaneous hemodilution with fluid containing native plasma protein completely restores blood volume in 48 to 72 hours. Studies of less than 24 hours would therefore seem to be inadequate and perhaps ideally they should be carried to 72 hours. In order to avoid expecting too much of an expander, experiments using plasma under the same conditions are necessary as controls, and saline also forms a good control as a relatively inefficient expander.

METHODS

Healthy male students between the ages of 19 and 27 have served as experimental subjects. They were admitted to the hospital where normal hydration was maintained on an oral fluid intake at a rate of 100 c.c. per hour during the studies.

Control measurements of hematocrit, hemoglobin, total plasma protein concentration, and plasma volume were made at the outset after which 900 to 1,100 c.c. of blood was removed rapidly (within 30 minutes) from a femoral artery. A blood sample was then taken for hemoglobin and hematocrit after which 1,000 c.c. of a plasma expander was infused intravenously in 30 minutes. Blood samples for determination of hematocrit, hemoglobin, total serum protein concentration, and expander concentration were withdrawn at 15 minutes, 4 hours, 12 hours, and 24 hours after completion of the infusion. In addition the plasma volume was redetermined at 4 and 12 hours postinfusioin. Where possible the urinary excretion of the expander has also been measured.

The Evans blue dye method was selected to determine the plasma volume and an effort has been made to obtain the most accurate results possible. Neither lipemia nor hemolysis was encountered in any case. The dye injected was measured by weighing the syringe before and after delivery, and dye concentration in plasma was determined on doubly centrifuged specimens using a Beckman spectrophotometer. Each patient's own plasma was used together with weighed amounts of dye to standardize the curve. Blood samples were drawn at 15, 30, and 45 minutes after injection of the dye and plotted to permit extrapolation to injection time. In the case of the initial plasma volume determination, samples were drawn at 15, 25, 35 and 45 minutes after dye injection. All samples were obtained from an indwelling arterial needle to avoid completely any stasis or variability in hematocrit.

Hemoglobin was determined on 1 c.c. volumes of blood as cyanomethemoglobin on an Evelyn colorimeter. Hematocrit was determined in Wintrobe tubes using 30 minutes' centrifugation at 4,000 r.p.m. with a centrifuge head of 26 cm. diameter. Total plasma protein was determined by a Kjeldahl semimicro technique as was also the concentration of oxypolygelatin. In the latter case trichloracetic acid precipitation was used to precipitate plasma protein. In the calculation of results it was assumed that the packed red cells contained 4.5 per cent trapped plasma. All samples were drawn into 10 c.c. syringes wet with heparin and we have determined that this results in dilution of specimens with 0.17 c.c. of heparin for which we have corrected in the calculations.

In the absence of direct determinations of red cell mass perhaps one should refrain from calculation of whole blood volume since it has been established that the hematocrit of blood in large vessels is not representative of that in the body as a whole. However, total body hematocrit has been compared with large vessel hematocrit by a number of investigators with surprisingly uniform results[3-6] showing that the former is just over nine-tenths of the large vessel hematocrit. One particularly complete study was done by Gibson and co-workers[3] in 40 healthy young men. When a trapping factor of 5 per cent is introduced into their figures we find that the ratio is 0.922 ± 0.038 (one standard deviation). This ratio held over a rather wide range of hematocrit values.

Data on blood volume and red cell mass for our subjects have been calculated on the basis of Gibson's figure. Reported hemoglobins and hematocrits are also calculated to represent total body figures. An estimated plasma and blood volume for 15 minutes postinfusion is also given. No new dye was injected at this point so this calculation is made from protein concentrations and is based on the assumption that no additional protein is lost from the blood stream after completion of hemorrhage and that none is added in the first 15 minutes. The 15 minute blood volume can also be calculated by the same dilution principle using hemoglobin figures. The calculated blood volumes by the two methods were almost identical in most instances.

RESULTS AND DISCUSSION

The data from the first 9 human experiments is presented in this preliminary report.

Four subjects have been given oxypolygelatin (OPG), three isotonic saline, and two plasma. Oxypolygelatin is an osseous gelatin which is fluid at room temperatures and is supplied as a 5 per cent solution in isotonic saline* thus making the over-all solution hypertonic. The plasma used was drawn especially for these studies with heparin as an anticoagulant thus avoiding the dilution which is present in ordinary bank blood drawn into citrate solution. The 1,000 c.c. lots of plasma were pooled from five donors.

In Table I are shown the data on total circulating hemoglobin and protein. Figures for individual experiments to show variability and its statistical analysis

*Supplied by Baxter Laboratories, Inc., Morton Grove, Ill.

will be given in a future communication after more cases have been added. Some idea can be gained, however, of over-all results to date from the column titled "mean hemoglobin" which shows, at least, that there is no large systematic error in the methods. If the conversion factor for large vessel to total body hematocrit is omitted from the calculations, the figures in the "mean hemoglobin" column are reduced by about 3 per cent. Others[1] have also shown that little if any new hemoglobin is added to the blood stream in the first 12 hours either from pools or as a result of new blood formation. It would appear from the table that native plasma protein was added to the circulation much faster in the subjects receiving OPG than in those receiving saline. This may be real or may represent inaccurate protein determinations in the presence of OPG.

TABLE I. TOTAL CIRCULATING HEMOGLOBIN AND SERUM PROTEIN AT INTERVALS AFTER HEMORRHAGE AND INFUSION

	HEMOGLOBIN*				PLASMA PROTEIN*		
	OPG	PLASMA	SALINE	MEAN	OPG	PLASMA	SALINE
15 min.	104	103	100	103			
4 hr	113	98	98	105	120	94	104
12 hr.	108	109	100	105	116	101	109

*Data for both hemoglobin and protein represent per cent of total amount in circulation at end of expander infusion.

Table II shows the plasma volume at intervals after the infusions. The data are expressed as per cent of the postinfusion volume. It can be seen that following either plasma or OPG a relatively stable plasma volume is maintained and there is nothing to choose between them on this basis in the cases so far. However, in the saline experiments, the saline was rapidly lost from the blood stream so that the plasma volume had fallen to only 88 per cent of its theoretical postinfusion value within 15 minutes from the end of the infusion or about 45 minutes from the beginning of the infusion. This represents a loss of approximately 500 c.c. or half of the volume infused.

TABLE II. PLASMA VOLUME AT INTERVALS FOLLOWING HEMORRHAGE AND REPLACEMENT BY OPG, PLASMA, OR SALINE

	PLASMA VOLUME (PER CENT OF POST INFUSION VOLUME)		
	OPG	PLASMA	SALINE
15 min.	99	104	88
4 hr.	102	98	87
12 hr.	96	104	89

The location of OPG at the various intervals after its infusion are shown in Table III. Here the data are given in percentage of the amount infused. It will be noted that within 45 minutes from the beginning of the infusion and 15 minutes after its completion, some 35 per cent of the OPG was lost from the blood stream, about 10 per cent having extravasated and 25 per cent having been excreted in the urine. Thereafter the rate of extravasation and excretion

slowed considerably. This is believed to be due at least in part to a variability of particle size of the OPG preparation, so that after the smaller particles are lost the rest remain longer in the circulation.

TABLE III. THE FATE OF OPG AT INTERVALS FOLLOWING HEMORRHAGE AND INFUSION

	LOCATION OF OPG (PER CENT OF INFUSED)		
	CIRCULATING	EXCRETED	EXTRAVASCULAR
15 min.	65	24	11
4 hr.	37	46	17
12 hr.	25	53	22
24 hr.		55	

SUMMARY

Nine healthy young male subjects have been studied before and after a rapid 1,000 c.c. hemorrhage and its replacement by oxypolygelatin, plasma, or saline. No effects on red cell storage, production, or destruction were demonstrable in this preliminary group. Native plasma protein was added to the circulation rapidly in the patients receiving saline or OPG and it seemed to be added more rapidly in the OPG group. The duration of intravascular retention and urinary excretion of OPG was quantitated and while OPG was rapidly eliminated initially, plasma protein was added sufficiently rapidly to maintain a practically stable blood volume. The patients who received plasma also maintained a good blood volume but those who received saline lost about half of the volume infused within 15 minutes of the completion of the infusion.

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DISCUSSION

DR. JONATHAN E. RHOADS.—I would only like to say that Dr. Barker outlined this approach to the subject and the report is preliminary chiefly because it is contemplated that a number of other plasma volume expanders will be compared by it. We think it is the most direct approach to comparing these expanders in patients which has been available so far and we are looking forward with a good deal of interest to seeing how the various dextrans, polyvinlypyrrolidone, and some of the newer gelatins will compare with oxypolygelatin. It would appear that we are not without substances which will stay within the circulation long enough to permit the body, at least the body of a person in fair health, to replenish its circulating plasma protein, but it is a difficult thing to choose between these substances.

Another factor which I think has to be kept before us is that nearly all tests of plasma volume expanders are being carried out in hemorrhagic hypotension or hemorrhagic hypovolemia, whereas, if a mass disaster occurs, we will be called upon to treat a very large number of thermal injuries. The thermal injuries are much more difficult to study. As far as I can see, it is impossible to study them under controlled conditions in man and we know now that one cannot transpose, with any confidence, results in experimental animals, for instance the burned rat, to man. It seems likely, therefore, that we shall have to persist with studies of hemorrhagic hypotension in comparing these agents and then, after that, obtain some clinical experience in burns which will not permit accurate comparisons but which will give some over-all impression of the general effectiveness of each agent. That has been done by Dr. Everett Evans in the case of dextran and in the case of ossein gelatin, and it has been done by Thorsen and Rosenqvist in the case of Swedish dextran. There remains a great deal of work to be done in this broad field and we believe the approach to it that Dr. Barker and his colleagues have employed is a valuable one.

DR. BARKER (Closing).—I would like to thank Dr. Rhoads for his comments. I might just mention that we did not present data regarding blood pressure effects of the 1,000 c.c. hemorrhage, but the mean arterial pressure of these subjects losing 1,000 c.c. in half an hour did drop almost uniformly by at least 20 or 30 points, and a good many of them had mild gastrointestinal symptoms. The blood pressure came back up rapidly and the symptoms disappeared with just a few hundred cubic centimeters of replenishment by any of the substances, including saline.

THE DANGER OF ADMINISTERING PARENTERAL FLUIDS BY HYPODERMOCLYSIS

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ALTHOUGH peripheral vascular collapse and oliguria occasionally result from the subcutaneous, subfascial, or intramuscular injection of an electrolyte-free solution, many physicians are not aware that such serious difficulties may occur following this procedure. On the other hand, periodic reports have appeared in the medical literature advocating the administration of a 5 to 10 per cent carbohydrate[1-3] or amino acid solution[4] by hypodermoclysis* or a 5 per cent dextrose solution intraperitoneally.[5] Thus, although the administration of parenteral fluids by hypodermoclysis has been accomplished many times without lasting or serious ill effects, it seemed pertinent to reappraise the problem especially in view of some of the newer solutions that are being used today (5 to 20 per cent invert sugar solutions and carbohydrate and amino acid mixtures with and without fat emulsions and various minerals).

The objectives of this study were: (1) to re-emphasize the dangers which might result following the extravascular injection of fairly large amounts of a solution devoid of inorganic electrolytes, (2) to demonstrate the change in the plasma volume following a hypodermoclysis of a solution of 5 per cent dextrose and of a 10 per cent invert sugar in distilled water,† (3) to determine whether the undesirable transfer of fluid and electrolytes could be modified or prevented by the use of hyaluronidase.

MATERIALS AND METHODS

Studies reported here were carried out on seven patients. Two of the patients were elderly women who had undergone abdominal surgery at the University Hospitals of Cleveland. Because of complications, parenteral alimentation was necessary, and since many of their veins were thrombosed or collapsed hypodermoclysis was resorted to. The patients were seen in consultation at this time and the fluid intake and output charts and blood studies were subsequently obtained from the hospital records.

The third case was that of a 19-year-old girl who had been admitted to the Medical Service of the University Hospitals of Cleveland because of nausea and intermittent vomiting of several weeks' duration. A thorough investigation

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*The term hypodermoclysis will be used to indicate the subcutaneous, subfascial, or intramuscular injection of fluid, although the administration of fluid was done by the subfascial route in the experiments reported here. From the standpoint of osmotic equilibrium, and the passage of fluid and electrolytes through a semipermeable membrane, the type of the reaction is similar, although the rapidity and severity of it may vary according to whether a solution is injected subcutaneously, subfascially, intramuscularly or intraperitoneally.

†The 10 per cent invert sugar in distilled water (Travert) employed in this study was kindly supplied by Dr. Robert P. Herwick, Medical Director of the Baxter Laboratories, Inc., Morton Grove, Ill.

TABLE I. A 69-YEAR-OLD WOMAN* WHO EXHIBITED OLIGURIA AND HYPOTENSION DUE TO HYPODERMOCLYSES OF 5 PER CENT DEXTROSE

Date (1950): / Postoperative Day:	PREOP.	(8/18) OP.	(8/19) 1	(8/20) 2	(8/21) (A.M.)	(8/21) 3 (P.M.)	(8/22) 4	(8/23) 5	(8/24) 6
Intake									
Oral		0	0	0	0	0	0	0	380
5% dextrose in normal saline (intravenous)		200	500			1,500	500	500	
5% dextrose in distilled water (intravenous)		1,600	1,500			1,000	2,700	2,800	900
Blood (intravenous)		1,000							500
5% amino acids in distilled water (intravenous)								1,000	1,000
5% dextrose in distilled water (hypodermoclysis)			1,000	3,000	2,000				
Total intake		2,800	3,000	3,000	4,500		3,200	4,300	2,780
Output									
Urine		850	600	200	60	415	2,300	3,700	3,200
Gastric suction		200	300	50					
Common duct tube drainage		120	150	125	100		125	50	100
Emesis		80	150	300	200		100		
Wound drainage (estimated)†		50	200	350	500		300	150	100
Insensible loss (estimated)†		1,200	1,000	1,400	1,600		1,200	1,000	1,000
Approximate total output		2,500	2,400	2,425	2,875		4,025	4,900	4,400
Balance		300	600	575	1,625		−825	−600	−1,620
				+3,100				−3,045	
Blood studies									
Hemoglobin (per cent normal)	73			98					85
Plasma protein (concentration Gm./100 c.c.)	6.2			6.9			5.3		6.0
Plasma chloride (concentration meq./L)	102.0				80		87		96

*Diagnosis: acute suppurative and chronic cholecystitis with cholelithiasis, acute pancreatitis. Operation: cholecystectomy and choledochotomy, Aug. 10, 1950. Complication: wound disruption, closure on Aug. 18, 1950.

†The daily estimates were made and upon adding up the intake and output totals and calculating the balance it was interesting to note how close the amount of fluid retained, during the first four days, came to the balance for the recovery phase. While the estimates may be questioned it seems apparent that the patient had received adequate water but because of the sodium deficit could not maintain a sufficient quantity of it in the extracellular compartment.

failed to reveal any organic lesion and her symptoms were thought to be on a functional basis. Ten days after admission, at which time the patient did not appear dehydrated, a hypodermoclysis was given because of a small emesis (30 to 60 ml.) on several occasions the previous day. The plasma volume was determined before and after the administration of 5 per cent dextrose solution, and periodic determinations of the pulse, blood pressure, and plasma protein and chloride concentrations were made.

The fourth to the seventh patients included in this study were four apparently physically well, mildly schizophrenic men, who had been committed to the Cleveland State Hospital for psychiatric care.* These subjects were given a hypodermoclysis of 10 per cent invert sugar on two occasions at weekly intervals. No food or fluids were permitted for 10 hours preceding, or during, the study. The patients were confined to bed while the observations were being made, but were permitted to change positions and occasionally to sit up. After completion of the study they were encouraged to drink tomato juice and other liquids. Determinations similar to those in the preceding case were done, as well as plasma sodium and potassium concentrations. A week later similar studies were performed with the exception that 150 turbidity reducing units of hyaluronidase† were injected through the hypodermoclysis tubing at the beginning of the infusion.

The plasma volume was determined by the injection of a known amount of radioactive iodinated (I^{131}) albumin. The technique of this procedure has been previously described.[6] The Beckman DU spectrophotometer with the flame photometer attachment was used for determining the plasma sodium and potassium concentrations. The plasma chloride concentrations were determined by the method of Schales and Schales.[7] Heparin was used throughout as the anticoagulant and the cell volumes (hematocrits) were calculated after centrifugation of heparinized blood in Sanford-Magath tubes at 2,500 r.p.m. for 30 minutes.

RESULT AND INTERPRETATIONS

The fluid intake and output and blood chemistries summarized in Tables I and II occurred during the postoperative courses of the two elderly women. While the blood pressure fell only slightly in one patient and moderately in the other following the hypodermoclyses, the temperatures, which had previously been elevated, fell to subnormal levels and their skins became cold, moist, and somewhat cyanotic. Oliguria was marked in view of what appeared to be an adequate daily fluid intake. Although recovery occurred, both patients were seriously ill at the time, and had death resulted, few persons would have ascribed it to the hypodermoclysis of a 5 per cent dextrose solution, although subsequently this was demonstrated to be the cause of the oliguria and hypotension.

In Table III the changes are summarized which followed the giving of 2,000 ml. of 5 per cent dextrose in distilled water by hypodermoclysis to the 19-year-old girl. Hypotension and tachycardia gradually developed and the pa-

*Arrangements for performing these studies were made possible by the generous cooperation of Dr. M. B. Gordon, Superintendent of the Cleveland State Hospital.

†Supplied through the courtesy of Dr. I. C. Winters, Director of Clinical Research, G. D. Searle & Co., Chicago, Ill.

TABLE II. A 67-YEAR-OLD WOMAN* WHO DEVELOPED OLIGURIA FOLLOWING A HYPODERMOCLYSIS

Date (1951): Postoperative Day	(3/31) 19/12	(4/1) 20/13	(4/2) 21/14	22/15 (4/3) A.M.	22/15 (4/3) P.M.	(4/4) 23/16	(4/5) 24/17	(4/6) 25/18	(4/7) 26/19	(4/11) 30/23
Intake										
Oral			180					115	1,490	1,875
Intravenous										
5% dextrose in normal saline	1,000	1,000								
5% dextrose in distilled water	2,000	2,000			2,000	1,300	2,300	1,000		
Blood					1,000					
Plasma (double strength)					250			250		
5% amino acid and 5% dextrose						800	600	2,900		
Hypodermoclysis										
5% dextrose in normal saline			1,000							
5% dextrose in distilled water			2,000							
Total daily fluid intake	3,000	3,000	3,180		3,250	2,100	2,900	4,265	1,490	1,875
Total daily potassium intake (meq.)	40	40	40		60	40	60	80		
Total daily sodium chloride intake (Gm.)	9.0	9.0	9.0		0	1.8	8.9			
Output										
Urine	1,700	2,000	100	175	3,000	3,500	3,250	1,500	500	750
Gastric tube suction		150	150	300	500	380				
Blood studies										
Hemoglobin (Gm./100 c.c.)		14.0		12.0			13.0			
Serum proteins, total (Gm./100 c.c.)				5.9		6.1	5.3	5.4	5.8	
Blood urea nitrogen (mg./100 c.c.)			6.0	12.0		7.5	8.3	22	12	13
Serum chloride (meq./L.)			86	79		85	82	83	87	93
CO_2 vol./100 c.c.			69				91	86	77	78
Sodium (meq./L.)			137.0				131.4		138.2	141.8
Potassium (meq./L.)			2.35				2.71		2.78	3.32

*Diagnosis: acute suppurative appendicitis with perforation. Operation March 12, 1951. Complications: paralytic adynamic ileus, wound disruption with closure on March 19, 1951.

tient complained of nausea and vomited several ounces of a bile-stained fluid an hour after the hypodermoclysis had been discontinued. She was restless for several hours afterward, during which time her blood pressure was subnormal. While the amount of fluid injected was more per kilogram of body weight (44.25 ml.) than in the four male subjects (23.8 ml., 24.9 ml., 32.2 ml., and 40.0 ml. per kilogram of body weight) her thighs never were as tense and full as when the 10 per cent invert sugar solutions were employed. In spite of the fact that she consumed food and water in the late afternoon and evening (a total fluid intake during the day of more than 2,500 ml.) and had no further vomiting, she did not pass any urine for almost 20 hours. This is quite a contrast to the volume of urine that would be expected if the same parenteral fluid had been given intravenously. The plasma volume in this patient decreased 433 ml., or 21 per cent. The increase in the hematocrit and plasma protein concentration and decrease in the plasma chloride level offer further evidence that a reduction of the plasma volume definitely occurred. A decrease in the total circulating plasma proteins also resulted.

TABLE III. THE EFFECT OF A HYPODERMOCLYSIS OF A 5 PER CENT DEXTROSE SOLUTION*

TIME FROM START OF INFUSION	BLOOD PRESSURE (MM. HG)	PULSE	HEMATOCRIT (PER CENT CELLS)	PLASMA VOLUME (ML.)	PLASMA PROTEIN (GM./100 ML.)	PLASMA CHLORIDE (MEQ./L.)
Control	98/66	80	42.3	2025	7.20	110.0
2,000 ml. given in three and one-half hours (0.21 ml. per kg. per min.)						
Three hours	94/70	86	43.5		7.61	105.5
Five and one-sixth hours	78/56	118	46.0		8.81	
Six and one-quarter hours	70/0	120	49.0	1592 (−21%)	8.46	100.2

*D. R., age 19 years.

The findings following the hypodermoclyses of a 10 per cent invert sugar solution are summarized in Tables IV to VII. The second series of determinations (lower half of Tables IV to VII) were obtained one week after the first studies. It was assumed that the subjects had returned to normal levels by this time. This assumption is supported by the fact that the control studies done at the start of each experiment were essentially the same although obtained one week apart. It will be seen that the decrease from the control plasma volumes varied from 244 to 820 ml. (10 to 31 per cent). In these four subjects frequent determinations of the pulse showed an increase in the rate but not as marked an increase as that seen in the first three cases, nor as great as one would anticipate. Since the plasma concentrations of sodium, potassium, and chloride showed slight changes all the results are not included in the tables. The decrease in the plasma volume was not consistently as great as would be expected in view of the rise in the hematocrit and the degree of hypotension that was encountered.

Oliguria or anuria was present during the six hours the subjects were studied and for at least the same length of time after the last determination was

TABLE IV. THE EFFECT OF A HYPODERMOCLYSIS OF A 10 PER CENT INVERT SUGAR SOLUTION*

TIME FROM START OF INFUSION	BLOOD PRESSURE (MM. HG)	HEMATOCRIT (PER CENT CELLS)	PLASMA VOLUME (ML.)	PLASMA PROTEIN (GM./100 ML.)	PLASMA CHLORIDE (MEQ./L.)
Control	126/82	42.8	3420	6.45	110.0
2,000 ml. given in three and one-third hours (0.119 ml. per kg. per min.)					
Three and one-half hours	128/88	54.0		6.67	109.4
Five hours	130/84	54.0	3040 (–11%)	7.30	106.0
Control	128/78	44.2	3260	6.86	109.0
2,000 ml. given with hyaluronidase in one and one-sixth hours (0.335 ml. per kg. per min.)					
Two hours	120/80	50.1			108.2
Five hours	108/90	55.0	2920 (–10%)	7.85	107.0

*R. B., age 23 years.

TABLE V. THE EFFECT OF A HYPODERMOCLYSIS OF A 10 PER CENT INVERT SUGAR SOLUTION*

TIME FROM START OF INFUSION	BLOOD PRESSURE (MM. HG)	HEMATOCRIT (PER CENT CELLS)	PLASMA VOLUME (ML.)	PLASMA PROTEIN (GM./100 ML.)	PLASMA SODIUM (MEQ./L.)
Control	134/72	40.8	2348	6.58	140.0
2,000 ml. given in three and one-sixth hours (0.214 ml. per kg. per min.)					
One and three-quarters hours	140/90	51.5		6.56	
Four hours	110/74	55.8	1930	7.60	136.0
Five hours	96/66	58.0	(–18%)	6.78	
Control	132/72	45.7	2390	6.46	104.3
2,000 ml. given with hyaluronidase in 40 min. (1.0 ml. per kg. per min.) (plasma chloride meq./L.)					
One and one-third hours	112/82	56.0		7.30	100.7
Three and two-thirds hours	124/88	58.5		7.92	98.6
Four and two-thirds hours	96/70	58.4	1656 (–31%)	7.35	96.4

*H. S., age 24 years.

TABLE VI. THE EFFECT OF A HYPODERMOCLYSIS OF A 10 PER CENT INVERT SUGAR SOLUTION*

TIME FROM START OF INFUSION	BLOOD PRESSURE (MM. HG)	HEMATOCRIT (PER CENT CELLS)	PLASMA VOLUME (ML.)	PLASMA PROTEIN (GM./100 ML.)	PLASMA POTASSIUM (MEQ./L.)
Control	170/92	44.0		6.65	4.33
2,000 ml. given in two and one-third hours (0.227 ml. per kg. per min.)					
One and two-thirds hours	168/100	46.5			
Three and one-sixth hours	142/92	50.5			
Five hours	136/96	51.5		7.60	4.15
Control	162/92	42.8	3030	6.76	143.0
2,000 ml. given with hyaluronidase in one and one-half hours (0.363 ml. per kg. per min.) (plasma sodium meq./L.)					
One and one-half hours	120/92				
Two hours	50/0	53.0		7.78	
Three hours	86/74	55.7		8.05	141.9
Four hours	92/74	59.0		7.95	
Five hours	106/82	55.6	2210 (–27%)	7.80	138.9

*H. T., age 59 years.

made. This occurred although the oral intake of water (in food and liquids) plus the hypodermoclyses provided an intake near or slightly above 3,000 ml. during the 12 hours.

The injection of hyaluronidase through the tubing and into tissues immediately after the hypodermoclysis was begun permitted the invert sugar solution to run in at a more rapid rate than was otherwise encountered. The fluid diffused over a somewhat greater area and thus caused less discomfort. Since the hypotension and the clinical signs and symptoms of peripheral circulatory collapse (cold, pale, moist skin, restlessness, anuria, etc.), as well as the changes in the chemical determinations were more marked when hyaluronidase was used, and because of other studies that will be subsequently reported,[8] it is felt that the maximum fluid shift was greater and occurred somewhat earlier when this enzyme was employed. Thus the height or severity of the reaction is apparently greater the more rapidly the fluid is injected, although the duration of it is somewhat shorter since the rate of absorption is increased due to the greater diffusion of the solution.

TABLE VII. THE EFFECT OF A HYPODERMOCLYSIS OF A 10 PER CENT INVERT SUGAR SOLUTION*

TIME FROM START OF INFUSION	BLOOD PRESSURE (MM. HG)	HEMATOCRIT (PER CENT CELLS)	PLASMA VOLUME (ML.)	PLASMA PROTEIN (GM./100 ML.)	PLASMA SODIUM (MEQ./L.)
Control	138/78	51.0	2576	6.65	147.0
1,750 ml. given in three and one-sixth hours (0.130 ml. per kg. per min.)					
Two hours	136/90	52.8		6.69	
Three and one-half hours	140/98	56.5		6.95	
Five hours	132/94	62.0	2332 (–10%)	7.75	142.0
Control	130/74	47.8	2495	6.95	103.0
1,750 ml. given with hyaluronidase in one hour (0.429 ml. per kg. per min.) (plasma chloride meq./L.)					
Two hours	122/80	58.8		8.97	104.5
Three hours	108/90	58.2		8.35	102.0
Five hours	108/88	55.5	2188 (–12%)	7.78	97.0

*D. A., age 22 years.

DISCUSSION

Most workers are in agreement that under many circumstances fluids can be given by hypodermoclysis without serious consequences. However, it has not been adequately emphasized that a serious situation may result when relatively large volumes of an isotonic solution, containing little or no inorganic electrolytes, or a hypertonic solution is employed. Since the patients can be made much worse, especially when a pre-existing dehydration, salt deficit, or hypotension exist, it is important to remember that when the administration of fluids by hypodermoclysis would be most helpful because of inaccessible veins (owing to repeated usage or peripheral circulatory collapse), the administration by this technique is likely to produce the severest and most detrimental change.

Some observers[1, 4] have added phenolsulfonephthalein to the fluid to be administered by hypodermoclysis and have concluded that the amount of dye recovered in the urine was approximately proportional to the volume of fluid absorbed from beneath the fascia. Since the rates of exchange across tissue membranes of water, inorganic electrolytes, sugars, and amino acids differ, it obviously is not valid to assume that phenolsulfonephthalein would measure the rate of absorption of any one or any combination of these constituents.

Numerous investigators have stated that the administration of fluid by hypodermoclysis or intraperitoneally is essentially the same. While some slight variations may exist, it is now evident that the same general conclusions can be applied to both modes of administration. Since the intraperitoneal administration of 5 per cent dextrose and the giving of a variety of solutions by hypodermoclysis has been advocated, a knowledge of the exact alterations resulting from such injections is essential if one is to prescribe fluids intelligently. In order that one may better understand the changes produced by a hypodermoclysis, some of the important contributions of the past will be briefly reviewed.

In 1894 Starling and Tubby[9] observed that an interchange of constituents took place between fluid placed in the pleural cavity and the blood in surrounding vessels so that "each took from the other that constituent which it did not possess." These workers also observed that when hypertonic sugar or salt solutions were injected into the pleural cavity it resulted in a copious flow of fluid into the cavity and that only after osmotic equilibrium was reached did the absorption of fluid progress slowly.

Putnam,[10] in 1923, reaffirmed Starling and Tubby's findings and emphasized that hypertonic dextrose solutions injected intraperitoneally were poorly borne. He stated that "they increased markedly in volume and much albumin appeared in them." He also stated that "the speed of diffusion of different molecules through the peritoneum appeared to vary inversely with their respective sizes." Thus, the rate of passage of inorganic electrolyte molecules through a semipermeable membrane is faster than dextrose which in turn is faster than albumin or the larger protein molecules (globulin, fibrinogen, etc.).

Schechter,[11] in 1931, undertook studies to determine the changes that took place when various fluids were injected into the peritoneal cavity or subcutaneous tissues. He concluded that dextrose solution injected intraperitoneally into guinea pigs draws in fluid from the plasma and interstitial spaces and that "a dry condition of the musculature" resulted. He concluded that "the principles of absorption from the subcutaneous tissues are presumably the same as from the peritoneal cavity and, therefore, the same general objections to the subcutaneous use of glucose hold."

Darrow and Yannet[12] demonstrated that the water of the red cell increased following the decrease in extracellular electrolytes indicating that the transfer of water was an important factor in "adjusting the osmotic equilibrium between plasma and erythrocytes." Yannet and Darrow,[13] Mellors, Muntwyler, and Mautz,[14] and Elkinton, Winkler and Danowski,[15] showed by tissue analysis that an acute loss of extracellular electrolyte resulting from the intraperitoneal

injection of dextrose caused little change in total body water, but was found to be accompanied by a transfer of water from the extra- to the intracellular compartment.

In 1946, Danowski, Winkler, and Peters[16] emphasized that a hypodermoclysis should not be administered until a pre-existing fluid and electrolyte deficit had been corrected and shock had been treated. They also stated that dextrose solution may intensify the salt deficit of diabetic coma if given subcutaneously.

Although it has been suggested[11, 17] that the principles of absorption of dextrose solutions from the peritoneal cavity and from the subcutaneous tissues are essentially the same, Danowski, Winkler, and Elkinton,[18] in 1947, proved conclusively that such was actually the case. Peters and Van Slyke[19] have stated that "glucose diffused more slowly than either water or salt across the envelopes of red blood cells, vascular membranes, and even through the interstitial spaces." It is apparent that if an isotonic dextrose solution is injected intraperitoneally or by hypodermoclysis, the volume of the injected fluid would increase somewhat as it became slightly hypertonic because of the relatively slower diffusion rate of glucose. This would result in a decrease in the extracellular fluid volume.

An additional loss of plasma and interstitial fluid would take place because of an intracellular shift of water resulting from the hypotonicity of the extracellular electrolytes. This intracellular shift of water may also cause some swelling of the red cell.[12, 20] This may account for the increase in the hematocrit which we often observed to be greater than would be expected from the plasma volume decrease.

When a hypertonic solution is given by hypodermoclysis the extraction of both fluid and electrolytes from the plasma and interstitial fluid compartments would occur. Although larger amounts of water would shift into the injected fluid than when an isotonic dextrose solution was employed, the loss of electrolytes should be even greater. The fact that we did not encounter sizable decreases in the concentration of sodium and chloride is difficult to explain in the light of our present knowledge. It is possible that the low electrolyte concentrations were increased somewhat because of the intracellular shift of fluid.

Webb, Lemmer, and Elman[21] not only confirmed Schechter's work, but by leg measurements showed that various solutions were absorbed from the thighs of patients at a rate somewhat comparable to the rate the same solutions were absorbed from the peritoneal cavity of the guinea pig. They also demonstrated that 5 per cent dextrose and 5 per cent amino acid in Ringer's solution led to an influx of fluid intraperitoneally with a resulting dehydration of the body tissues. It would appear, therefore, that in many instances the administration of a solution low in, or devoid of, electrolytes regardless of its organic constituents may produce sizable shifts of fluids and salts from one compartment to another.

No ill effects were noted by Weinstein[4] when he gave a hypodermoclysis of a protein hydrolysate or by Shafiroff, Baron, Richt, and Mulholland[22] when they administered solutions of emulsified fat containing 5 per cent dextrose and

5 per cent amino acids. In all probability no apparent difficulty was observed by the aforementioned workers owing to the fact that for the most part relatively small volumes of these solutions were given to fairly healthy subjects.

The rate of absorption of a solution depends upon the similarity of its composition to interstitial fluid, its tonicity, the molecular size of the solutes and, among other things, the extent of the surface area of the fluid in contact with the absorbing membrane. Hyaluronidase, because it causes the solution to diffuse over a greater area, increases the rate that fluid can be administered and probably accelerates absorption. The fact that the solution diffuses more widely would lessen tissue tension and pain, but hyaluronidase might well intensify the undesirable reaction of a hypodermoclysis because it does permit large quantities of fluid to run into the tissues very rapidly. Since the reaction would be greater the faster the solution is injected it might be preferable to omit hyaluronidase, or to administer the fluid very slowly or in small quantities intermittently when hyaluronidase is employed.

Butler and Talbot[23] state that "since only solutions given intravenously should contain more than 2.5 per cent dextrose, provision of sufficient dextrose by clysis to provide the basic calories is impracticable." They point out that to accomplish this by hypodermoclysis without employing hypertonic solutions or solutions devoid of electrolytes would necessitate giving an excessive amount of water and salt. Thus it would appear that in most instances the maximum benefits and least derangement to the normal body fluid compartments can be accomplished by giving parenteral fluids by the intravenous route.

Although fluids may be given by hypodermoclysis with or without hyaluronidase, these experiments should emphasize the possible dangers which might be encountered when large volumes of sugar- or amino-acid-containing fluids are given in this fashion, especially to sodium-deficient or hypotensive patients.

CONCLUSIONS

1. When a 5 per cent dextrose or a 10 per cent invert sugar solution is administered by hypodermoclysis a transient water and salt depletion of the extracellular fluid compartment occurs.

2. Sizable decreases in the plasma volume were shown to result from the shift of fluid presumably into the site of injection and into the intracellular space.

3. Such alterations are likely to be encountered when hypertonic solutions are used or when isotonic solutions very low in, or devoid of, inorganic electrolytes are given.

4. Oliguria, anuria, and circulatory collapse may result from a hypodermoclysis of an electrolyte-free solution, especially in patients with incipient shock or in dehydrated or salt-deficient individuals.

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BLOOD VISCOSITY AND THE WHOLE BLOOD THERAPY OF BURNS

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INTRODUCTION

IT IS unusual nowadays for a burned patient under hospital care to die of shock secondary to inadequate blood volume. There is ample evidence, however, that volume replacement alone is not enough. The composition of the fluid replacement is as important as its quantity, both in the acute phase and in the weeks to follow.

Modern knowledge of the fluid requirements of a burned patient is based upon clinical observation and laboratory measurements, both of which are subject to wide variation in interpretation. Underhill[25] demonstrated the importance of blood volume based on the change in hematocrit. Simultaneous studies of burn edema and the circulating blood have shown that a protein-rich plasma filtrate leaks rapidly into the burned area.[8] Estimates of the effect of a burn upon circulating red-cell mass, formerly inferred from dye dilution and hematocrit data, are now being measured by using isotope-tagged red blood cells. In our experience with radioactive iron and chromate methods[15, 20] only 7 to 10 per cent of the red-cell mass is destroyed initially by a 35 per cent full-thickness burn, and this volume of red cells is replaced by transfusion. The plasma and electrolyte loss is far greater proportionally, and plasma is therefore the predominant colloid given.

Other groups studying burns have advocated whole blood transfusions as the major initial colloid replacement in burns. Their studies indicate that survival time in dogs is prolonged, that the severity of postburn anemia in patients is reduced, and that the hemodynamics in the patients may be improved by early therapy with whole blood.[1, 12, 14, 16] Measurements of red-cell mass, using radioactive phosphorus, show much larger losses than with iron and chromate methods.[17, 22] Trapping and pooling of red cells are postulated which, together with hemolysis, create a red-cell deficit.

Obviously, if the predominating loss from the circulation is a dilute plasma, and if the colloid element of this loss is replaced with whole blood, such therapy will tend to maintain the elevated hematocrit seen in an untreated burn. The significance of an elevated hematocrit to the circulation then comes into question.

It has been shown that the viscosity of whole blood rises in proportion to the hematocrit.[5-7] In studies upon other forms of shock Seligman,[23] Richards,[21] Price,[19] and Wood[27] have considered the effects of high-hematocrit blood upon the circulation and have intimated that high viscosity may be harmful, particularly under conditions of reduced blood flow.

Because of disagreement concerning the relative volumes of plasma and red cells lost we have measured the effects of various combinations of fluid therapy in patients and in dogs. And, because viscosity measurements have not been

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applied directly to studies on burns, we have investigated the measurement of blood viscosity and the significance of altered blood viscosity to the dynamic qualities of the circulating blood.

BLOOD VISCOSITY

In simplest terms, the viscosity of a liquid is defined as its internal resistance to molecular rearrangement when it is disturbed. This quality can be measured in a capillary tube under conditions of laminar flow. The unit of measure, the poise or centipoise, is defined as the force required to move one of two parallel planes past another when the space between the planes is filled with the liquid to be tested. Finally, the rate of fall of a sphere through the liquid provides the basis for Stokes's law concerning viscosity. The design of the various apparatuses used in measurement coincides roughly with these three concepts of viscosity.[3]

Liquids, such as water, with simple molecular structure behave in a predictable manner under experimental conditions. The more complex the liquid or mixture, the more varied is its intermolecular bonding and its behavior during flow.[4, 18] It becomes necessary then to define the fluid behavior of a very complex mixture such as blood by comparing it with water under the same conditions. The Hess capillary viscosimeter is best suited to this purpose. It consists of two pipettes with capillary segments in their mid-portions, so calibrated that the rate of flow of water is the same in each when suction is applied to them simultaneously. Experimentally, the standard pipette is filled with water, the other with the liquid to be tested. Although consistent results are obtained, they are only an expression of behavior relative to water under the conditions of the experiment and cannot be transposed into absolute units of measurement for the following reasons:

1. *Temperature.*—Most liquids flow more rapidly as they become warmer but they do not all change in the same proportion.[5, 11, 24] A correction curve must be constructed for simultaneous comparison of blood and water at varying temperature and hematocrit values. Within the temperature range of our experiments (24 to 28° C.) the correction factor was found to be less than 0.2 unit of viscosity.

2. *Suction.*—Complex colloidal suspensions possess properties of elasticity and "yield values" which severely limit the conditions under which flow and viscosity are predictable. Their flow is called anomalous for this reason.[7, 10, 26] In the range of hematocrit of our experiments a vacuum of 5 cm. Hg was most practical and was used throughout. Increasing the vacuum to 7 cm. Hg reduced the viscosity less than 0.4 unit while adding significantly to the technical error of the measurement.

3. *Capillary Diameter.*—When very small capillary tubes are used, the viscosity figure of blood tends to decrease, whereas flow in large tubes may not be laminar. The pipettes used here are within the limits of size found most accurate by other workers.[6, 13]

4. *Miscellaneous.*—CO_2 content of the serum and added anticoagulants affect the measurements.[6, 9, 10] After standardizing the anticoagulant (heparin) we found the correction for the CO_2 content to be less than 0.2 unit.

Our preliminary studies on dog and human blood showed that the viscosity of serum or plasma varies directly with the protein concentration. Variations due to hemolysis and altered albumin-globulin ratio are insignificantly small. Similarly, whole blood viscosity varies primarily with the hematocrit, although plasma protein concentration is reflected in the measurement. These findings coincide with those of previous workers.[5-7]

CONDITIONS AND CONDUCT OF THE EXPERIMENTS

Healthy mongrel dogs were anesthetized with intravenous Nembutal. The lower thorax, abdomen, and hindquarters were clipped. The bladder was catheterized for continuous urine collection. The brachial and carotid arteries and jugular vein were exposed. A Cournand needle was placed in the brachial artery and attached to an electromanometric recording device. Blood samples were taken by free flow from a major artery or vein. Blood removed for sampling was replaced. Burning was done by immersing the dog from the hind feet to the xyphoid in hot water (85 to 83° C.) for 12 to 30 seconds. After burning, the dog was covered with a blanket. At death or sacrifice, a gross inspection of the organs, the burn, and the vessels was made. Treatment was given into the cephalic vein. The dogs showed no evidence of experiencing pain.

Control periods of ½ to 3 hours were run following induction of anesthesia. Values were measured initially and just prior to burn. The time from the burn to the onset of treatment was varied from 10 minutes to 3 hours. Values were measured simultaneously at intervals of 1 to 2 hours after the burn. A period of 10 to 20 minutes was allowed for circulatory adjustment and mixing before sampling. Anesthesia was kept at a moderately deep level by clinical standards. Experiments were limited to 10 to 12 hours to minimize the effects of clostridial toxins.[2]

The values recorded were hematocrit and whole blood viscosity; serum protein and serum viscosity; temperature (rectal), pulse, and respirations; blood pressure and arterial pulse wave tracings; urine flow; and nonprotein nitrogen.

In burned dogs hemolysis of red cells colors the plasma and adds inaccuracies to the measurement of plasma volume by the T 1824 dye method. To avoid confusing the effects of low blood volume with those of altered blood composition it was essential that treatment be volumetrically adequate to replace losses into the burn. This matter was resolved by varying the total quantity and rate of therapy given. In the experiments the range was 5 to 18 c.c. per kilogram per hour from the time of burn to the end of the treatment period. All previous evidence indicates that the losses due to the burn described should fall within this range.

The effects of anesthesia alone, of a severe untreated burn, and of burns treated with saline, plasma, or whole blood in various proportions are recorded.

RESULTS

A. *Anesthesia Control* (Two dogs)

1. The variations in temperature, pulse, respirations, and blood pressure decrease as the deeper levels of anesthesia are approached.

2. The other values show a 3 to 5 per cent variation over the experimental period. Urine output decreases slowly if no fluid is given.

B. *Untreated Burn* (Fig. 1) (In 7 dogs the results are classical.)

1. The control period is shown.
2. There is a progressive rise in temperature, pulse, and respirations.
3. The urine output decreases. The increase in nonprotein nitrogen averaged 15 mg. per 100 c.c.
4. The blood pressure gradually declines, and bizarre changes are seen in the pulse wave tracing as the circulation fails.
5. The hematocrit and whole blood viscosity rise steadily.
6. The serum protein and serum viscosity increase.

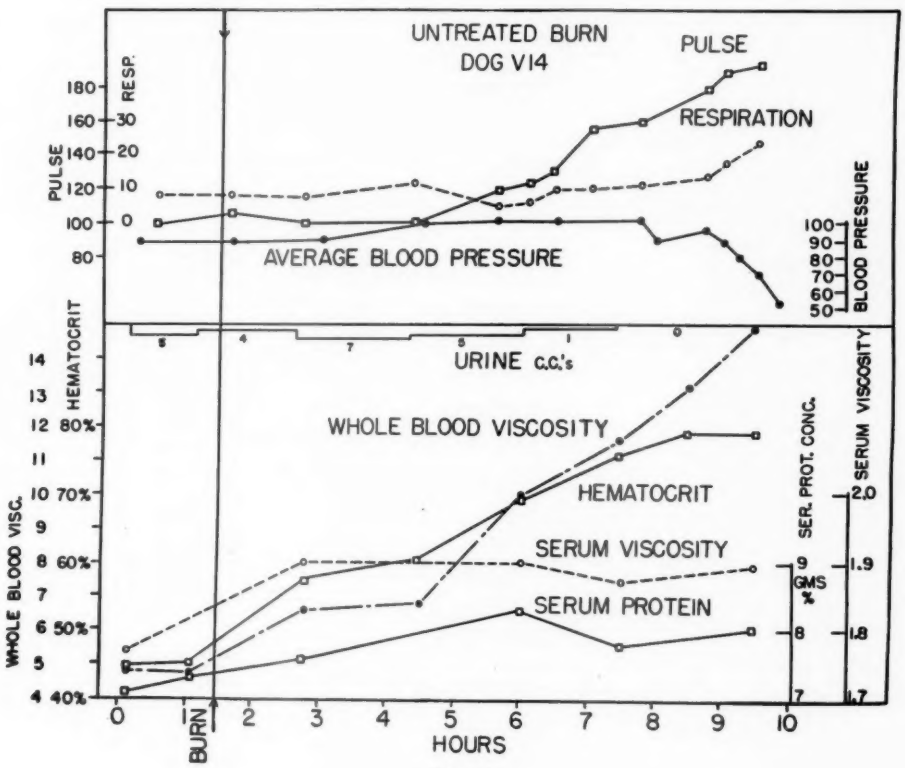

Fig. 1.

C. *Saline and Plasma Therapy*

1. In three animals saline was given alone. In three others it was combined with plasma in ratios of 2:1, 1:1, and 1:1.5.
2. Volumes given ranged from 5 to 17 c.c. per kilogram per hour.
3. Fig. 2 shows:
   a. The predominance of saline therapy which produced a progressive decrease in serum protein. Gross edema of the unburned tissues was evident at autopsy.
   b. A rate of 8 c.c. per kilogram per hour was inadequate to replace loss into the burn as indicated by rising hematocrit and diminishing urine flow. Doubling this rate apparently produced volume replacement.

c. The viscosity values followed the hematocrit and serum protein as before.

4. Other facts borne out in the six dogs were:

a. The urine output is maintained, the nonprotein nitrogen does not rise, and the blood pressure and pulse waves are normal when replacement is volumetrically adequate.

b. When plasma predominates over saline in the therapy the serum protein value does not decrease, and the unburned tissues do not become edematous.

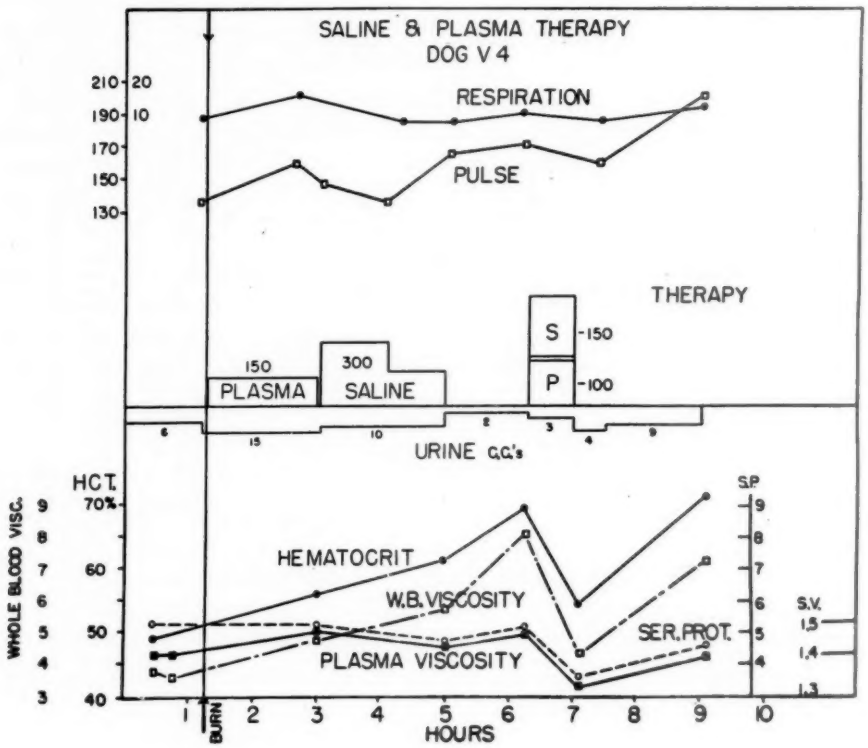

Fig. 2.

D. *Whole Blood Therapy* (Five dogs)

1. In five dogs the quantity of therapy was varied from 5 c.c. per kilogram per hour to 18 c.c. per kilogram per hour. Blood was combined with saline in ratios varying from 2:1 to 1:2.

2. Fig. 3 shows treatment at a rate of 8 c.c. per kilogram per hour, and in a ratio of 4:3 with saline.

a. There is a progressive rise in hematocrit and whole blood viscosity. The serum values are unchanged.

b. The urine output is maintained. The nonprotein nitrogen rose slightly in this dog but not in the others.

c. The blood pressure and pulse waves are not significantly changed.

3. This was the pattern of change in all the animals of this group. When the quantity of saline given exceeded that of whole blood, the serum protein concentration fell as in the saline- and plasma-treated dogs.

SUMMARY OF RESULTS OF ANIMAL STUDIES

In the 20 experimental animals the results support the concept that protein-rich plasma filtrate is the major loss from the circulation into a burn wound. The viscosity values vary directly with the hematocrit and serum protein values in the burned animal as in the pilot studies. The treatment with whole blood is accompanied by rising hematocrit and viscosity values.

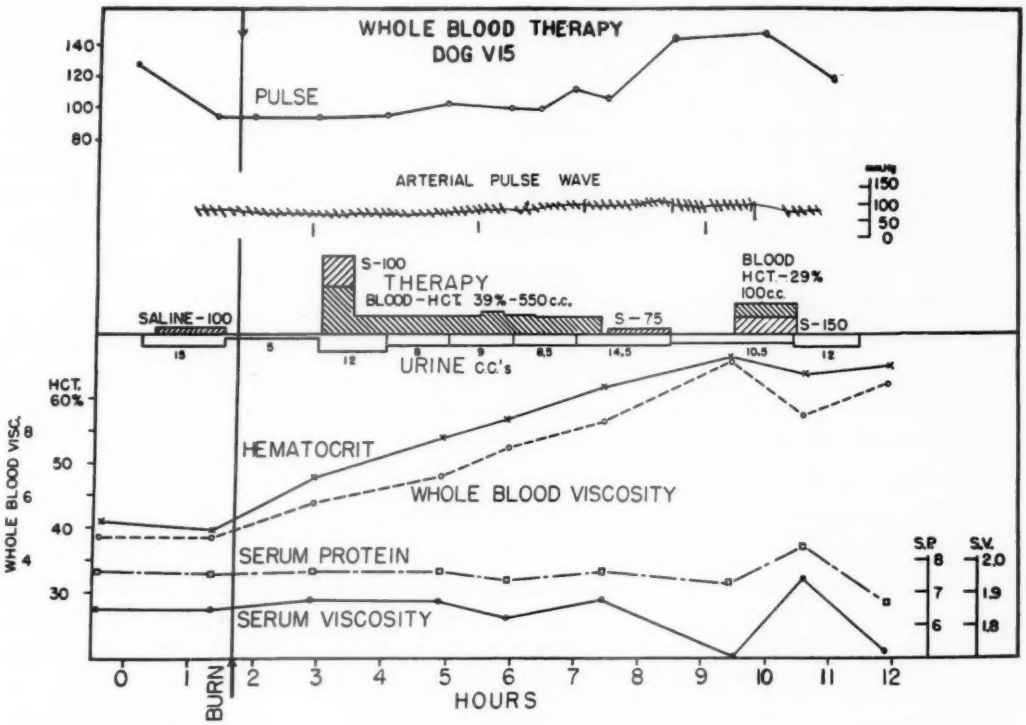

Fig. 3.

Twelve of thirteen dogs receiving treatment were alive and strong 8 to 10 hours after burn and were sacrificed. Five of seven untreated dogs also survived this period but obviously were much sicker than the treated ones at sacrifice.

SUMMARY OF STUDIES IN PATIENTS

Viscosity measurements were made in 6 severely burned patients, 4 of whom were treated predominantly with plasma and 2 with whole blood as the only colloid given. Nonprotein nitrogen, serum protein, hematocrit, blood and serum viscosities, and urine flow were recorded at frequent intervals. As in the dogs, the viscosity paralleled the hematocrit and serum protein concentration.

In the two patients where whole blood was the only colloid therapy and was combined with saline and dextrose solutions in proportions of 1:6 and 1:2, the

hematocrit rose to 70 per cent within 12 hours, as in the experimental animal. Although the hematocrit continued between 60 per cent and 70 per cent for 3½ days, with proportionately elevated viscosity, no adverse effect was demonstrable by clinical standards. In both of these patients the hematocrit and viscosity were normal about 1 week after burn, while one showed severe sepsis and moderate anemia at 4 weeks in spite of continued transfusions.

The patients treated predominantly with plasma and electrolyte solutions (500 c.c. of blood customarily were given on the second day) also showed a pattern similar to the experimental animals and no adverse effects clinically.

DISCUSSION AND CONCLUSIONS

The laboratory and clinical experiences described show that saline therapy alone will not sustain the circulation in acute burns without producing generalized tissue edema. The proper combination of plasma and saline apparently maintains blood volume, and edema occurs only in the burned area. Substituting whole blood for plasma sustains blood volume and serum protein concentration but is accompanied by an abnormal concentration of red cells in the circulation. We conclude that our concept of the composition of burn edema fluid is substantiated, and that loss of circulating red-cell mass is small in proportion to loss of plasma.

We have found no consistent effect of the viscous blood upon the pulse rate and tracing, blood pressure, and kidney function. In recent experiments we have added oxygen utilization studies to determine whether abnormal viscosity may produce effects upon tissue metabolism that are not reflected in circulatory dynamics. These will be described in a subsequent paper.

The premise that treatment should maintain normal values of blood volume and constitution has proved valuable in managing the acute phase of fluid shifts in the burned patient. In our experience there is great variation in the measurable effects of a burn early in the course, while developing sepsis makes interpretation more difficult later on. The significance of the survival time of dogs or of the severity of anemia in patients must be qualified by such facts. We conclude that the therapeutic premise is sound, and that a closer agreement among measurements made by the newer techniques is required before transposing the results into therapeutic terms.

SUMMARY

1. The nature, the methods of measurement, and the significance of blood viscosity are reviewed.

2. The concepts which govern fluid therapy of burns in the acute phase are discussed and tested by measuring the response of patients and dogs to treatment with saline, plasma, and whole blood.

3. The viscosity of whole blood varies directly with the hematocrit value, serum viscosity primarily with serum protein concentration.

4. Colloid replacement with whole blood in adequate quantity maintains or augments the high hematocrit and viscosity values seen in an untreated burn.

5. Using standard techniques of measurement of pulse rate and tracing, blood pressure, and kidney function no remarkable effects of abnormal viscosity were shown in the dogs or in the clinical course of the patients.

We acknowledge with gratitude the technical assistance of Miss Ruth L. Moore and Mr. Walter L. Turner.

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DISCUSSION

DR. WILLIAM E. ABBOTT.—Since I am one of the individuals who advocated the use of whole blood transfusions for the shock treatment of patients following a thermal injury I think that there are a few things that should be clarified regarding this presentation.

Most of us who have employed this type of treatment during recent years have noted that hemoconcentration can be prevented or corrected when whole blood is administered, providing adequate amounts of an electrolyte solution are given. The balanced electrolyte solution we advocated seven years ago had a chemical make-up similar to that of interstitial fluid and, subsequently, since it was felt that additional water was necessary, a two-thirds isotonic solution was given to adults in amounts varying between 2,000 and 10,000 c.c., depending on the severity and type of the burn (first and second degree burns required less blood than deep second or third degree burns). In 25 to 30 patients and in numerous animal experiments hemoconcentration continued to increase on only two occasions following the onset of therapy. In both instances it was encountered when inadequate amounts of the electrolyte solution were available to the body (lack of absorption or vomiting). Thus, it has become quite apparent that if from approximately 5 to 10 times as much of a sodium-containing solution as blood is given, hemoconcentration can be corrected or prevented.

From experiments which we briefly reported in 1944, it is evident that if one determines the increase in sludging and viscosity by Knisely's technique following various forms of experimentally induced hypotension, the viscosity is more affected by an increase in the protein constituents of the plasma than by concentration of the red cells.

The sludging and viscosity increased most markedly when dehydration was rapidly produced experimentally by injecting 5 per cent dextrose in distilled water intraperitoneally. To a slightly lesser degree it was apparent following experimental pyloric obstruction. In both instances the concentration of red cells was quite marked but the total plasma protein concentration rose to levels of 8.5 to 11.0 Gm. per 100 c.c. This increase was largely in the fibrinogen and globulin fractions and hence largely accounted for the increased viscosity and sludging. When a similar degree of hemoconcentration was produced by an experimental burn there was not nearly as pronounced a change in the viscosity or sludging. When hypotension resulted from an experimental intestinal strangulation neither the red cell nor protein elements increased and the increase in the degree of sludging and viscosity was again considerably less.

Since studies by Cope and Moore in 1944 demonstrated that albumin is lost as rapidly from the vascular system following a burn as is sodium, there seems little advantage in giving substances with the hope of increasing the osmotic pressure. It is evident that if albumin is lost the osmotic pressure outside the capillary will be increased and thus attract fluid to this region rather than increasing the plasma volume. While the protein molecules of larger molecular weight (globulin, fibrinogen, etc.) do exert some osmotic effect, they also markedly increase the viscosity.

Therefore it seemed that from the experimental and clinical studies "shock" was prevented or minimized not by raising the osmotic pressure of the plasma, but by increasing the tissue tension. Berman's experimental and clinical observations substantiate this view. Instead of depending on the orally ingested or intravenously infused solutions to leak out of capillaries into the burned area, he injected a normal saline solution into the region directly, and thus increased the tissue tension and prevented or corrected shock.

In using whole blood and an electrolyte solution properly, it would, therefore, appear that hypotension is adequately counteracted without adversely affecting the viscosity. In patients so treated it seemed to have the advantage of providing a better renal function, especially

during the first twenty-four to forty-eight hours, alleviating to some extent the anemia that is so apparent during the convalescent phase of a deep burn and causing an earlier regression or absorption of the edema in the burned region than in plasma-treated patients or animals.

Darrow stated in 1944 that a high red count per se was not a contraindication to the transfusing of blood. Since the concentration of red cells (25 to 35 per cent) in a bottle of blood which has had an anticoagulant added is considerably less than that seen in the vascular compartment following a thermal injury (40 to 75 per cent), hemodilution will take place following a transfusion. This is especially apparent if further fluid is prevented from leaking from the vascular system (by increasing tissue tension) and that already lost is replenished.

Therefore, in fairness to both schools of thought, the effect on viscosity of plasma-treated and of electrolyte solution (in proper amounts) and whole blood treated animals should be compared before any criticism is justified.

DR. QUINBY (Closing).—At the Massachusetts General Hospital our routine use of whole blood in the initial steps of burn treatment has been limited to replacement of red-cell deficiency. We have not been convinced that its use for replacement of plasma colloid was logical. Our concept of the use of whole blood is based on the studies made by Dr. Cope and Dr. Moore during World War II; plasma has been the principal colloid solution given. In our present work we are re-examining the question with new methods; thus far we have not found reason to change our point of view.

I believe that the physical quality of viscosity of the blood should not be emphasized in treatment unless it can be shown to affect the circulation or tissue metabolism significantly. Over a fairly wide range of values, including those near to the limits observed clinically, viscosity has not yet been shown to be harmful, but this is not to say that in patients with heart disease or in ranges not recorded here, viscosity may not influence the circulation unfavorably. Also, newer techniques may show that tissue metabolism is affected adversely. In our studies we are trying to measure alterations in the blood following burns, while in our therapy we are trying to prevent gross deviations from the normal. At the present time, our therapy is based upon the premise that normal blood values are desirable. Whether we are right or wrong remains for further study to show.

STUDIES IN CORTISONE

II. Metabolism in Cortisone Poisoning; Effect of Cortisone on Tissue Culture of Fibroblasts

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ALRICH, Carter, and Lehman[1] reported a study confirming and extending the earlier observations of Howes, Ragan, and others[2, 3] and demonstrated the profound retarding effect of large doses of cortisone on the healing of wounds in the rat, both by test of tensile strength and histologic study. The striking histologic changes consisted of retardation in the appearance of all the cellular elements of repair of mesenchymal origin. There was delay in the proliferation of typical fibroblasts and capillaries during the first six days and little production of collagen even by the twelfth day in the cortisone wounds as compared to the controls. Two new findings were a curious distribution of new capillaries and the presence of relatively large, round, clear cells similar to the "foam cells" of the central nervous system (Gitterzellen). The mechanism by which cortisone results in these changes was not investigated, although the work of others has suggested it is possibly a direct local effect on the tissue.

The present study was undertaken because of evidence that the rat may become adapted to cortisone in some respects, especially in regard to nitrogen balance.[4] It was hoped that in addition to determining whether the rat adaptation to cortisone would prevent the previously noted changes in healing, information in regard to the mechanism of these effects might result. It was planned to conduct metabolic balance studies of potassium, sodium, chloride, and nitrogen in a group of rats and, after possible adaptation to the dose of cortisone had occurred, test wounds would be made. Tensile strength and histologic studies would then be carried out as in the first experiment. As will be seen, this program had to be modified. Studies were carried out also on the effects of cortisone on tissue culture of fibroblasts in an effort to determine whether the cortisone effect was a direct one on the fibroblasts and whether the previously described "foam cells" could be reproduced in tissue cultures.

METHODS

For the metabolic studies Wistar strain rats 7 weeks old were used. The rats were fed for at least 1 week in stock cages a standard 22 per cent protein diet, with complete vitamin supplements before being placed in metabolic cages. The food cups in the metabolic cages, which were fitted with metal tops with small openings, were placed in glass jars to prevent the scattering of food. The

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food intake and weight of each rat were measured every 2 days to the nearest gram. Water was allowed ad libitum. The bottoms of the cages consisted of metal funnels coated with paraffin, in the top of which were screens on which the rats rested. Urine was collected every 2 days under toluene. Fecal contamination of the urine was prevented by a plug of fine screen wire in the neck of the funnel. Each collection day the funnels were washed with water after discarding the feces, and the urine and washings volume made up to 100 c.c. with distilled water. Aliquots of the urine were analyzed for nitrogen by the

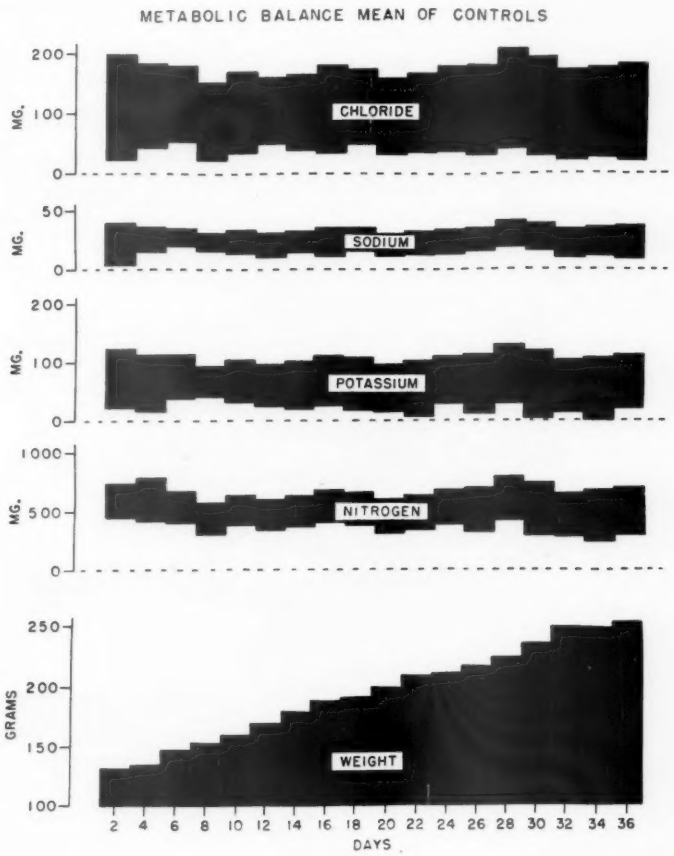

Fig. 1.—Metabolic balance. Mean of 2 control rats. (Method of charting: Intake charted from *0* upward; output charted from top of intake downward in black. Distance of black column above or below *0* indicates degree of positive or negative balance, respectively.)

Kjeldahl procedure, sodium and potassium by the flame photometer, and the chlorides by the Valhard technique. There were 3 groups of animals, a control group of 2, and 2 experimental groups of 12 animals each. One experimental group received 20 mg. of cortisone per kilogram of body weight and the other 15 mg. of cortisone per kilogram of body weight every 12 hours, subcutaneously, a daily total of 40 and 30 mg. of cortisone per kilogram of body weight, respectively, for 35 days after a control period of 1 week.

Tissue cultures of striated and cardiac muscle from the rat embryo were grown in roller tubes using balanced saline, serum, and embryo extract as

nutrient. A group of 40 roller tubes containing an average of 4 explants each that had grown only fibroblasts were selected after 24 hours' initial growth. These were divided into a control group of 10 tubes and 3 experimental groups of 10 tubes each. The experimental groups were treated with cortisone in concentrations of 25, 50, and 100 μg per c.c., respectively, by adding the hormone to the nutrient. The latter was replaced every 2 days.

A second group of 24 roller tubes were selected after 24 hours' initial growth, regardless of whether there was a growth of epithelial cells, fibroblasts, or both. These were divided into a control group of 10 tubes and two experimental groups of 7 tubes each. The experimental groups were treated with

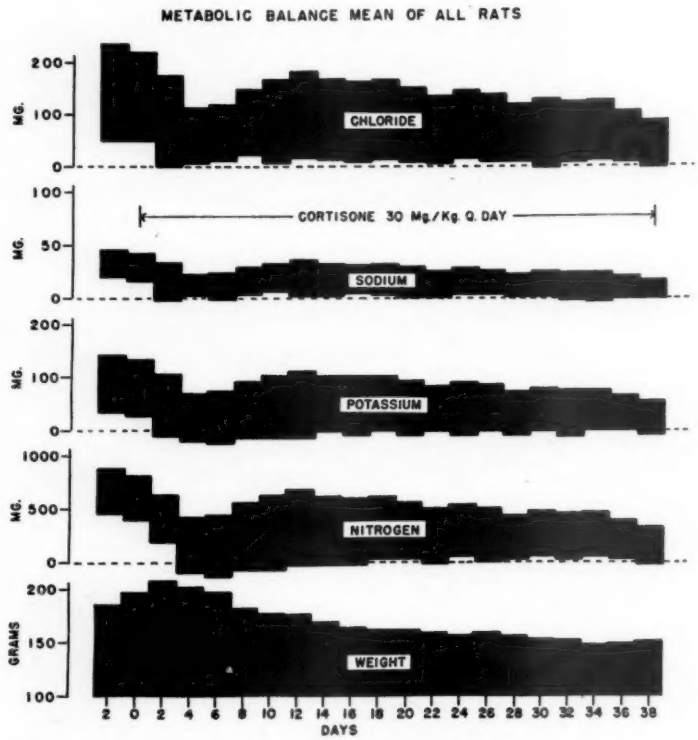

Fig. 2.—Metabolic balance. Mean of 12 rats, given 30 mg. of cortisone per kilogram of body weight per day. Control period indicated on the left. (For method of charting see Fig. 1.)

cortisone in concentrations of 50 and 150 μg per c.c., respectively, for 24 hours, by removing the nutrient and replacing it with cortisone solution in balanced saline. Following the 24 hour exposure to cortisone, the culture was exposed again to untreated nutrient which was changed at 2 day intervals.

RESULTS

The control rats and the rats in the metabolic study during the control period ate well and gained weight at a uniform rate. They remained in positive nitrogen balance (amounting to 100 to 200 mg. of nitrogen a day). They all also remained in slightly positive sodium, potassium, and chloride balance (Figs. 1, 2, and 3). Forty-eight hours after the experimental groups were placed on

cortisone (Figs. 2 and 3) there was a loss of appetite, as evidenced by a fall in the food intake. There was also a negative balance of all 4 food factors studied. This was followed by loss in weight and by lassitude of the animals. Within 4 to 16 days there was an increase in food intake which approached the level of food intake of the control period and a return to positive chloride, sodium, and nitrogen balance. Neither the amount of intake nor the degree of positive balance reached the levels of the control period. The potassium excretion remained high and even with the increase in food intake did not show a tendency to return to positive balance as did the nitrogen. The weight curve during this period showed a tendency to level off as compared with the initial rapid loss after cortisone was started, but there was a continued small loss in weight. After 22 to 26 days of cortisone the animals again began to eat less food and they were, by this time, emaciated.

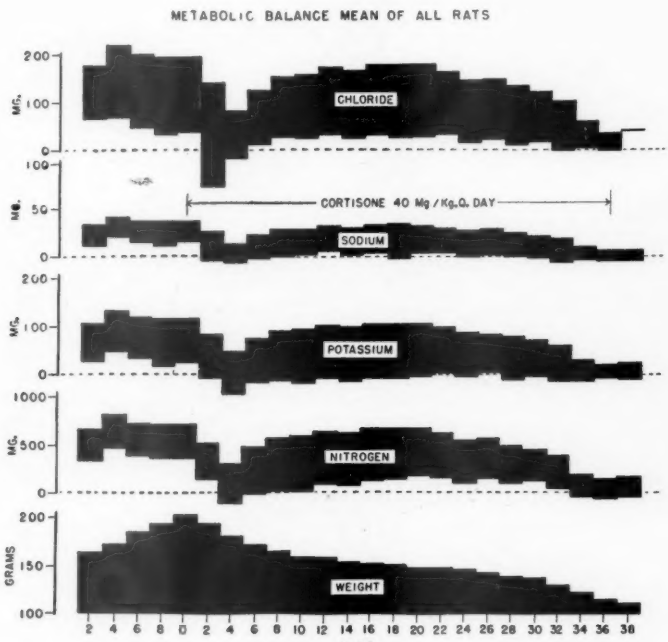

Fig. 3.—Metabolic balance. Mean of 12 rats, given 40 mg. of cortisone per kilogram of body weight per day. Control period indicated on the left. (For method of charting see Fig. 1.)

With the massive doses of cortisone the animals were in poor condition, and never became so adapted that the experimental wounds could be made. The earliest death occurred on the twenty-fifth day after cortisone was started in the group receiving 40 mg. of cortisone per kilogram of body weight, and by the thirty-sixth day, 8 of the 12 animals were dead. Even though the drug was discontinued, 3 of the remaining 4 animals died during the next 5 days. The one surviving animal was sacrificed on the twelfth day after cortisone had been discontinued. In the group receiving 30 mg. of cortisone per kilogram of body weight, the metabolic balances resembled closely those with larger dosage, and 4 of 12 animals died by the thirty-sixth day.

Although the pathologic studies of the animals are not complete, 2 findings should be noted. The adrenal glands were not demonstrable grossly except as minute dark spots in the adipose tissue above the pole of each kidney. Microscopic sections revealed a marked degree of atrophy of the cortical adrenal cells. The animals also showed extensive areas of pneumonia throughout both lungs with small abscesses. The predominate organism was a fungus which has not been definitely identified.

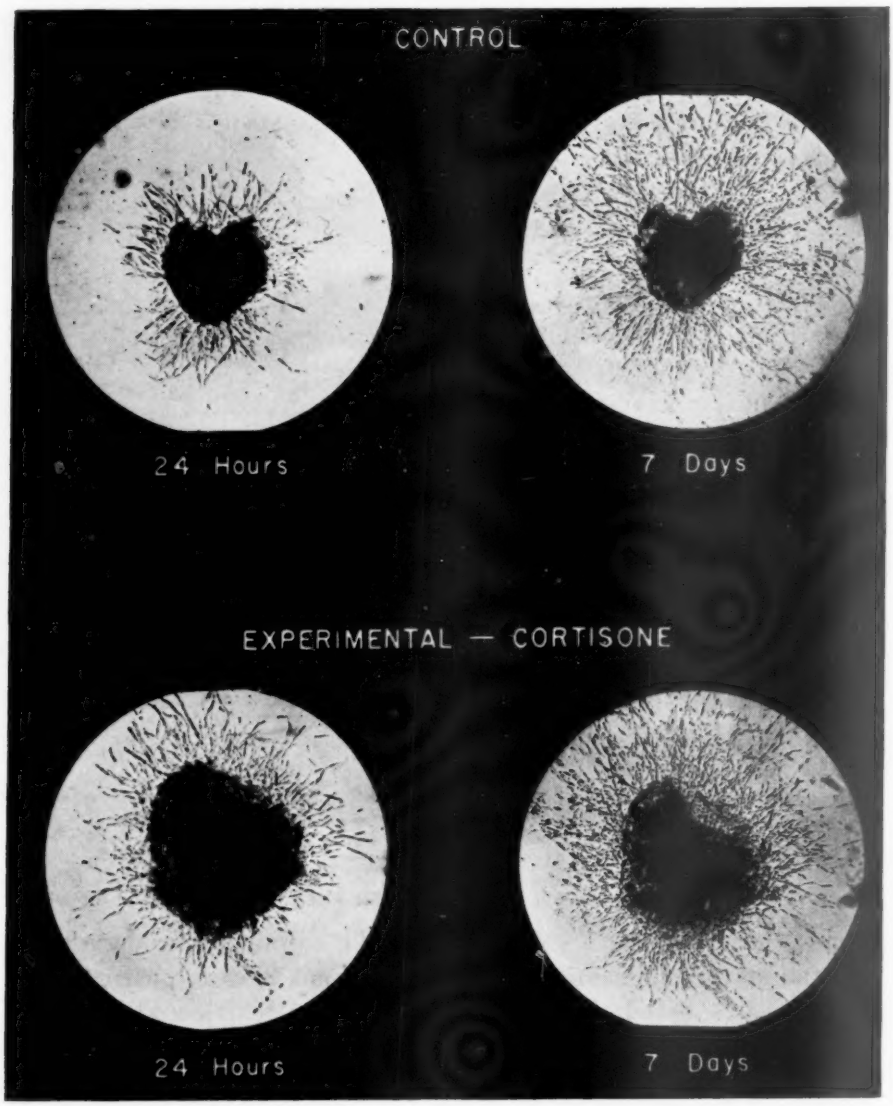

Fig. 4.—Tissue culture explant. Control and experimental cultures at 24 hours and 7 days (experimental 50 μg cortisone per c.c. in nutrient).

The tissue cultures, both control and experimental, grew well for a period of 7 to 12 days, developing a wide growth of elongated bipolar cells arranged in radiating strands or in irregular networks (Fig. 4). The character and amounts

of growth in the control and experimental groups were indistinguishable under the naked eye or with low- and high-power magnification. The histologic characteristics of the individual fibroblasts under higher power were uniform in both the control and experimental cultures. There were no cells produced by the explants in the experimental groups resembling the "foam cells" previously observed in healing wounds.

DISCUSSION

Cortisone in the high dosage used here causes in the rat marked alteration in electrolyte and nitrogen metabolism as well as depression of appetite. The animal tends to adapt quickly in the initial period of treatment in respect to appetite, sodium, chloride, and nitrogen metabolism, with a return to slight positive nitrogen balance being noted especially. However, this adaptation to the hormone is not demonstrated in the case of potassium, the excretion of which remains high and results in a negative balance during the period, while adaptation of the animal in respect to nitrogen is evident. It would therefore seem that the principal toxic effect of high dosage of cortisone may be the excessive excretion of potassium. The adaptation reported by Ingle[4] in regard to nitrogen balance may therefore be explained as either adjustment or the result of nontoxic dosage. Prolonged therapy with high dosage causes profound deleterious effects. Furthermore, these may result in, or at least be accompanied by, severe unresisted infections. In the studies of Antopol[5] in mice, the predominant organism was *Corynebacterium diphtheriae,* while in this series it was an unidentified fungus. The frequency of infection is, of course, the basis for providing antibiotic support for all patients on prolonged cortisone therapy and contraindicates cortisone therapy in the presence of infection.

Heilman[6] and Cornman[7] have suggested that adrenal steroids produce a direct selective effect upon fibroblasts in tissue culture. This study, like that of Baldridge and co-workers,[8] does not confirm their observations. The absence of effect on fibroblasts in our observations in tissue culture seems to indicate that the effect of high dosage of cortisone therapy upon fibroplasia in healing wounds is an indirect one.

SUMMARY

1. Cortisone administered to rats in large doses for a prolonged period results in marked adrenal atrophy and profound metabolic changes to which the organism is able to adapt only temporarily. The alterations in potassium metabolism are most marked and possibly are the cause of, or contribute to, the death of the animal.

2. As a terminal event, there is associated infection which is apparently resisted poorly by the animal.

3. Cortisone does not prevent growth, or change the character of the cells in tissue cultures of fibroblasts.

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THE EFFECT OF HEALTH INSURANCE PROGRAMS ON RESIDENCY TRAINING IN SURGERY

The Report of The Committee on Graduate Training in Surgery of The Society of University Surgeons

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THE training of surgeons by the residency system of graduated, increasing responsibility has proved conclusively to be the most satisfactory method of developing surgical knowledge and skill in young physicians since the system was instituted by Halsted so many years ago. Surgical training is unique in that, if carried to completion, it becomes dramatized by the fact that the trainee is allowed to perform what in the popular mind is considered to be the greatest personal therapeutic service—the operative procedure itself. It is granted that the operation is only one phase of the care of the patient, and may actually be overshadowed in importance by either the preoperative preparation or the postoperative care. It is of interest that the residency system, which has made it possible for the resident to perform the operative procedure upon indigent or semi-indigent patients, has developed and flourished as a result of a socioeconomic inadequacy. Now, with the growth of health insurance and a prolonged period of prosperity this socioeconomic inadequacy is being neutralized to the extent that the residency training system is being imperiled by a gradually decreasing volume of clinical material being available for the "service" beds.

The fact that this situation exists will need no proof to those who are interested in the maintenance of surgical training programs. The growth of hospitalization insurance which has been so phenomenal in the past ten years is being paralleled by medical service insurance which provides for the payment of a professional fee. In certain parts of the country hospitalization and medical service insurance have grown to such an extent that residency training has already been influenced. This is particularly true in the highly industrialized areas such as exist in Michigan, Rhode Island, and some areas of the South where a very high percentage of the workers have broad health insurance coverage. In other areas the problem is less acute, but critical inspection of service admissions makes it evident that insured patients are becoming more frequent and that the problem of what to do with the ward patient with medical service insurance is becoming more prevalent. A real problem faces those who wish to preserve the essential elements of the residency training system. The problem has many facets, and it seems important to reduce it for consideration to its basic elements in attempting to find a solution.

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Before progressing further, it is well to consider briefly other methods of surgical training and to decide whether the residency system is indeed worth preserving. It is true that many surgeons have developed well through preceptorships and assistantships, and these methods of training will probably continue to play a role in surgical training of the future. However, the superiority of a graduated residency system cannot be denied. It is emphasized by the requirements of the American College of Surgeons and the American Board of Surgery and by the great emphasis that has been placed on this type of training in all the major training centers of the country. Therefore, the assumption is made that it would be unwise to abandon efforts to retain the essential elements of the residency training system in view of the encroachment made upon clinical material by the growth of health insurance, and that any solution to this problem should aim at preserving the residency system by adapting its needs to the problems that have been presented by socioeconomic progress.

Regarding the types of hospitals and training programs that are affected by the growth of health insurance, it is well to break them down into groups in order that we may better understand the problem.

Veterans Hospitals.—Of the Veterans Administration Hospitals approximately 45 have approved residency training programs in surgery. These hospitals are an example of the type of institution that should be unaffected by the growth of health insurance. The patients presenting themselves for care at a Veterans Hospital are applying to an institution, not an individual. They have foregone the privilege of selecting their own physicians and they are entering an institution in which the policy of residency training under supervision has already been established.

City, County, and State Charity Hospitals.—Those charity hospitals with nonuniversity part-time staffs and with large resident staffs may be affected since it is obvious that with prosperity and with the growth of insurance there will be fewer patients in the completely indigent category. As a matter of fact, it is already evident that in many of the charity institutions of this type, the type of patient seen is becoming predominantly of the older age group and of the "skid row" variety. Fewer and fewer patients in the age groups compatible with economic self-support are being seen except as emergency admissions. This means that even in hospitals of this category there is developing a relative scarcity of certain types of clinical material desirable for training purposes.

Charity Hospitals Connected With City, County and State University Medical Centers.—Institutions of this category which depend predominantly upon the admission of completely indigent patients will probably be little affected for some time to come. These institutions fall into essentially the same category as those in the paragraph above. However, it should be kept in mind that the future may find even this category of patient completely eliminated through the development of some type of insurance which will provide not only for hospitalization for the patient, but remuneration for professional care. Such a situation now exists in the State of Washington where any indigent patient

can select his own physician and the physician can collect a fee from the State for caring for the patient. Any solution of the present problems should be aimed basically at the time when all patients will be covered by insurance.

University Medical Center With Full-Time Staff.—Since such institutions have made it the practice to integrate their residency training programs with the use of private as well as semiprivate and clinical material, it is unlikely that they will be adversely affected by the growth of hospitalization and medical service insurance. Actually, the growth of hospitalization and medical service insurance can be expected only to increase the number of patients coming to such institutions and thus to increase the quantity of clinical material which can be used in the residency training program. Such has been the case at the University of Chicago Medical Center which falls into this class.

University Medical Centers With Mixed, Full- and Part-Time Staff.—These institutions have either an appreciable quota of private beds or are in close association with other hospital buildings in which private beds are available. The element of competition for the insured case then comes in to complicate the picture. Here embarrassment of the residency training program will exist to varying degrees depending upon local custom and policy regarding the admission of insured patients to the ward training service. It can be said by the part-time men, who are depending upon the practice of surgery for at least part of their living income, that the institution is competing with them and indulging in the private practice of surgery if the institution accepts the insured case into its service beds. This can be a fatal hindrance to the acquisition of material for training and teaching purposes, especially if backed up by local and state medical society action. It is the training services falling into this category that will suffer most and present the greatest problem. It is of interest to note that this group includes many of the institutions that have been the backbone of the residency system in the past.

University Hospitals With Complete Part-Time Staff.—The problem can exist here to an even greater degree than in the institutions described in the category above and for the same reasons. Few university services of this type are left.

Nonuniversity-Connected Private Hospitals.—These institutions have always had a difficult time supplying adequate clinical material for residency training. Their troubles have been greatly added to by the marked growth of health insurance. A survey of a few hospitals of this category at the present time reveals them to be floundering in an effort to continue providing surgical training programs that will meet the standard necessary for approval. There is an increasing demand on their limited number of beds by private and semiprivate patients. The scarcity of the true service type of patient has resulted in devious efforts being made to use private clinical material for training purposes at many institutions. This is generally done without the patient's knowledge and presents a moral and ethical problem that is another facet of the over-all dilemma.

A questionnaire submitted to seventy-five surgical department heads in 1950 resulted in the accumulation of information from sixty replies. Only eleven institutions indicated that they had not detected an increase of patients with medical service insurance coverage in their service beds. Almost without exception these institutions were of the completely charity type.

Thirty-five replies indicated that no encroachment on the clinical material for training purposes had been detectable. This was explained in eighteen instances as being due to the fact that patients with medical service insurance were used in the residency training program. The remainder of the thirty-five, again, represented chiefly the purely charity institutions.

All but the purely charity institutions indicated that patients with medical service insurance were admitted to the ward beds of the surgical training service. Only seven replies indicated that it was the policy not to allow the patients with medical service insurance to be operated upon by the resident staff.

The methods of collection and disposal of the surgical fee provided by the insurance were as follows: To the university surgical department, ten; to the attending surgeon himself, seventeen; to the hospital, nine; collected by the attending surgeon and turned over to a departmental fund, seven; collected by a legal agency established for the purpose, one; fees uncollected, two.

Regarding the moral aspects of surgery being performed by members of the resident staff on patients with hospitalization and medical service insurance, only four replies indicated that there might be a definite objection. All remaining replies indicated that there was no objection to the residents performing the surgery provided that the patient was not misinformed, that the resident was adequately trained and supervised, and that the final responsibility for the welfare of the patient rested in a responsible senior member of the department.

In reply to the question as to what freedom should be allowed the patient with hospitalization and medical service insurance in the selection of his physician, it was indicated by the majority that such a patient should have complete freedom to select an institution or a group and that under such circumstances, once this selection had been made, the patient forfeited his right to select an individual member of the group.

It would seem that a policy should be established which will aim at resolving the conflict that exists between the shrinking number of charity patients seeking admission to training centers and the need of clinical material for training purposes. Although the problem pertains acutely to surgical training it is also of importance to all other branches of medical education, undergraduate as well as graduate. It is obvious that the problem exists largely because of the growth of various types of health insurance—voluntary, industrial, and local and state plans for insuring those who heretofore were not able to seek private care. In the philosophical consideration of this problem, it appears justifiable and necessary to project our thinking forward to the time when everyone may be covered by health insurance, either voluntary or otherwise, or a combination of different types. Whether or not we want to see this accomplished and whether or not we

oppose compulsory insurance and state control of the program is of no consequence to the present problem. Our concern is with the question of how we will continue to train surgeons when health insurance is universal, which it will be if its present rate of increase continues. If it is decided that the essential features of the residency system as it now exists are worth preserving, there are certain steps that might be considered.

First, a beginning might be made by the utilization of the clinical material that is now available to the fullest advantage. To accomplish this the state, county, and city charity hospitals should be used efficiently. This may mean affiliation and rotation between training centers that are being crippled by the growth of insurance and charity hospitals which still have an adequate supply of clinical material. The standards and the conduct of our present training services must be kept at such a level that admission to the service beds will continue to be sought because of the high caliber of professional care and personal attention that patients receive here. The Veterans Administration Hospitals with surgical training programs should be supported actively and used for surgical training. At the same time every effort should be made to correct abuses relative to the treatment of financially able patients with nonservice-connected disabilities. In these hospitals the policy establishing the use of clinical material in residency training is already crystallized and functioning. The drive to popularize surgical training services in some instances may justifiably extend to the point of improving the personal appearance of the resident staff which on a busy service can degenerate to a very disreputable level, if neglected. Perhaps the term "intern" should be dropped from our surgical training programs or be limited to that group of trainees who are in their first year out of medical school. It has been suggested that the resident surgeon might be elevated to an apparently higher rank by a change in his title and attire. All of these things might be considered to be of some value in exploitation of training material that is now available. However, it is obvious that they do not approach a solution to the basic problem which has to do with the encroachment on service beds of patients who are so covered by health insurance that they become of the private and semiprivate category.

Just why are patients with health insurance lost to the service beds? The answer to this problem is very complex and varies tremendously over different parts of the country. However, there seem to be three fundamental reasons why this result has been produced: (1) Not only are the insured patients being lost to the private practitioners through the patient's own volition, which is all well and good, but in some areas the teaching institution is not allowed to accept insured patients who apply to them for care. In some instances this has resulted from local custom and the action of the local and state medical organizations. (2) The insuring agencies have complicated the matter by the manner in which they insist that the statements be submitted and the fees collected. (3) The legal aspects of fee collection, income tax returns, and final disposal of the funds have presented problems that have contributed to delaying the solution.

The effect of local custom and tradition on this problem varies throughout the country to a remarkable degree. For instance, one teaching center which for years has been practicing as a full-time group and which is well accepted and entrenched in the community, finds that its clinical material has been greatly enhanced by the rapid growth of health insurance coverage. In this center, residency training has been accomplished through the use of private and semi-private patients as well as service patients for many years, whereas another training center with a partial full-time staff, and using a hospital with the predominance of service over private beds, is not permitted to admit any patient who has medical service insurance, even though that patient may have been referred to the medical center for a specific reason. This institution's surgical training program—and indeed its whole medical teaching program—is doomed unless this policy is changed. It is also of interest that, in one state, two hospitals in very close proximity geographically vary tremendously in the degree to which their training programs have been affected. One, a university medical center staffed by a predominance of full-time professional men has been affected only favorably. The other, a large private hospital which in the past had a large ward service is now reduced to only a small nucleus of its former service beds. It appears obvious that the hospital and training center with full-time professional staff will be able to continue with its training program unhampered by the present socioeconomic trend. Institutions of this nature have already established the principle that residency training can continue on insured patients. It certainly is not practical that, as an over-all solution, all hospitals with training services should adopt the full-time staff plan. However, it seems apparent that to meet the problem it will be necessary to establish the policy that insured patients *not be excluded* from training services simply because there is an insurance fee available for professional service.

One of the functions of the medical profession is to perpetuate itself by training new members in the best possible manner. This is a duty we owe to society. If the residency system of training in surgery is the best method of training surgeons then it is our duty to preserve its essential features in some manner. We are performing a duty to society in training surgeons to completion under supervision, rather than in turning them loose on the public to get their final training and experience unsupervised. Therefore, it seems justifiable to establish the principle that insured patients may be cared for by supervised residents in training, even to the point of the residents performing the major therapeutic procedure itself.

If this principle is accepted we are immediately faced with certain problems. Some of these pertain to the legal aspects of the procedure and are here considered as details that can be solved by various methods such as licensing the trainee, giving the trainee a staff appointment and changing his title, changing the policies of the insurance companies themselves which might hinder this method of working out a solution. The more important problems that are presented by adopting the policy that residents shall operate upon insured patients are the moral and ethical ones. What becomes of the patient's freedom

of selection? Is it not unfair for training centers to accept such patients and thereby compete with practicing physicians for the insurance fees that are available? Regarding the first of these questions, it seems that the patient should have complete freedom of choice within the limits of his ability to pay. If he has minimal insurance coverage and is of a low income bracket, he should also have freedom to choose to be cared for in a service bed of a medical training center. Here the importance of the maintenance of the high standard of professional ability on the training service becomes evident. Should a patient be barred from such a training service simply because he has a small amount of insurance for a professional service fee? Regarding the competition that will be practiced against the medical profession by the adoption of this policy, it seems that in order to fulfill its obligation to society in providing it with trained physicians and surgeons the profession is going to have to make certain concessions that will facilitate this training.

It is possible for insured patients to be utilized for surgical training without interfering with the patient's freedom of choice and without severely competing with the private practice of medicine and surgery. The patient can exercise his freedom of choice by accepting the treatment afforded through a ward service bed. Eligibility to these beds can be limited, among insured patients, to those whose income does not exceed a certain level. This level would probably have to vary throughout different parts of the country. It could be determined through collaboration between the training centers and the local organized medical profession. It might prove to be advisable to limit the number of insured patients admitted to ward training services to a maximum specified number for any one institution, which will serve the purpose of providing adequate teaching and training material. The intent is to supply clinical material for a very important purpose, not to procure revenue from the clinical material. It is even possible that nonuniversity private hospitals could solve some of their difficulties in maintaining recognized residency training programs by adopting a similar plan.

As it becomes more and more evident that in order to maintain the essential features of our residency training programs it will become necessary to use insured clinical material, we are brought face to face with the problem of what should be the disposal of the income from such patients. As was indicated in the questionnaire which has formed the basis of this study, this facet of the problem is far from a uniform solution. The majority of institutions which accept such patients on the ward services have provided for the funds thus collected to be returned to the university, the department of surgery, or to the hospital itself. This was accomplished through a variety of means including collection of the insurance by the department head; by the attending surgeon who then endorsed the fee over to the surgical department or university; and, in one instance, by a legal body established specifically to collect and administer this fund. Obviously, the details of solution of such a problem will vary tremendously with different institutions. Since the professional service insurance fees have been intended as remuneration for professional service it would seem that a logical disposition of funds from this source would be into

professional rather than administrative and service channels. Furthermore, the administration of such funds should be under the control of the surgeons in charge of the service. The needs for funds are many and it is quite easy to mention only a few outstanding ones which could absorb such funds: the pay for interns and residents per year has long been at a low level and might be supplemented by income from insurance; living, recreational, and library facilities can always absorb surplus funds. In general, it does not seem unreasonable to expect that the funds be used in some manner to further the interest of the training and teaching service other than in paying hospital cost which is a function of hospitalization insurance.

SUMMARY

The problems concerned with the continuation of the present residency system of training in surgery as a result of increasing hospitalization and medical service insurance have been discussed. It appears that in order to insure a continuing supply of clinical material to teaching and training services it will be necessary to establish the policy that such services be permitted to accept patients with medical service insurance to be cared for by members of the resident staff under attending staff supervision. This policy is already in effect in some institutions and should be adopted generally. A consideration of the moral and ethical aspects of this problem seems to indicate that it is not only justifiable but that it is a necessity if the medical profession is to fulfill its responsibility in training younger men. The income level of eligible patients as well as the disposition of the insurance fee are matters of detail requiring solutions which will vary with local factors.

RESOLUTION

The preceding report of the Committee to Study Graduate Training in Surgery was accepted by the Society of University Surgeons and the following resolution was passed:

WHEREAS, The Society of University Surgeons has as one of its primary aims the encouragement and development of surgical training, and

WHEREAS, The Society of University Surgeons believes the residency system of surgical training providing graduated responsibility under supervision to be the best method of training surgeons, and

WHEREAS, A residency system of graduated responsibility in surgical training requires the availability of clinical material to be cared for by resident surgeons under supervision, and

WHEREAS, The growth of medical service insurance is known to be curtailing the volume of clinical material available for surgical training because of loss of insured patients from ward training beds, be it,

Resolved, That the Society of University Surgeons continue its full approval of hospital and medical service insurance as a mechanism of improving medical care and opposing government-controlled medicine, but subscribe to the principle that patients with hospital and medical service insurance have the right to elect to be treated on ward training services, and that those of selected economic levels must be permitted on these services if the standards of surgical training are to be maintained.

EXTENSIVE SMALL BOWEL RESECTION IN YOUNG DOGS: ITS EFFECT ON GROWTH AND DEVELOPMENT

An Experimental Study

H. William Clatworthy, Jr., M.D., Richard Saleeby, M.D., and Charles Lovingood, M.D., Columbus, Ohio

(From the Department of Surgery and the Surgical Laboratory, Ohio State University College of Medicine, and the Surgical Service, The Children's Hospital)

THERE is an abundance of clinical and experimental evidence to justify the resection of up to 50 per cent of the small bowel in adults.[2, 3, 5, 9] However, in dealing with infants and children suffering from multiple or extensive lesions of the small bowel or its mesentery, surgeons have been justifiably hesitant to undertake resections of a similar magnitude, since there is no conclusive evidence that the growing child will adequately compensate for the loss of such a large portion of the alimentary tract. In certain instances—for example, meconium peritonitis and multiple congenital atresia—several resections of short segments of small bowel or numerous short-circuiting procedures have been carried out in order to conserve as much length and absorptive surface as possible. Similarly, some children with large nonmalignant growths of the mesentery have been denied the benefit of surgical extirpation for fear of injury to the blood supply of the major portion of the small bowel. In such instances, a single extensive resection would minimize the number of anastomoses, shorten the operation, and, of even greater importance, completely eradicate the primary pathology.

This experimental study in young dogs was designed, therefore, (1) to determine how much small bowel may be safely resected in a growing puppy, and (2) to evaluate the effect of such an extensive resection on the future growth and development of the animal.

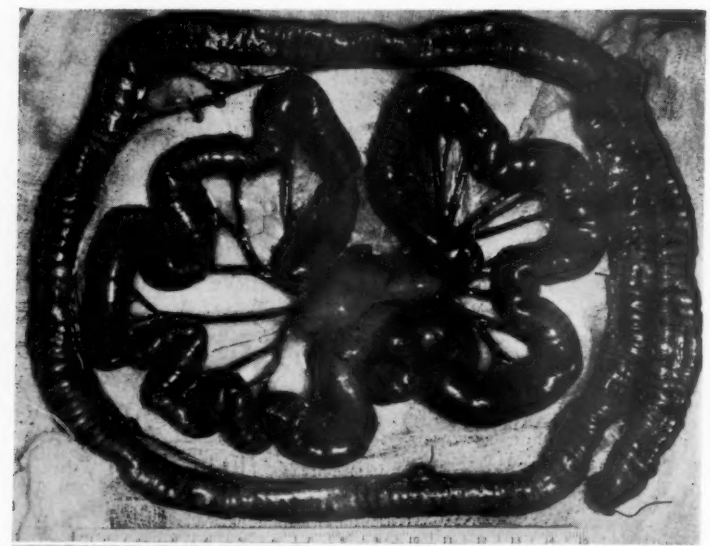
THE EXPERIMENT

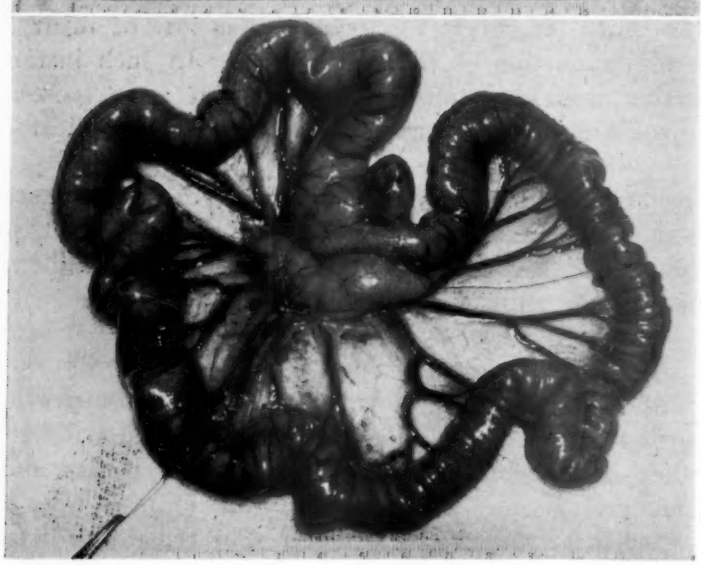
The dog was used as the experimental animal, because previous investigators have reported a close correlation between the results obtained following massive resection of the small bowel in adult human beings and adult dogs. Six litters of mongrel puppies totaling twenty-five animals were studied. One member from each litter served as a control. The remaining litter mates were subjected to an excision of 40 to 80 per cent of the small bowel. One of three types of resection was performed: jejunal, ileal, or mid-portional. The method of determining the per cent of resection was based upon: (1) the actual measurement of the length of the small bowel in situ as compared with the length of small bowel remaining, and (2) the total number of blood vessel arcades sacrificed compared to the number of arcades remaining. The length of the small intestine as measured in situ from the ligament of Treitz to the cecum

Read at the meeting of the Society of University Surgeons, Baltimore, Md., Feb. 7-9, 1952.

varied in these animals from 87 to 215 cm. A comparable variation in the over-all length of the small intestine in infants has been recorded by Robbins[8] and Bryant.[1] The number of primary mesenteric blood vessel arcades was remarkably constant and ranged between twelve and fourteen. The jejunal

A.





B.

Fig. 1.—*A*, A typical 60 per cent mid-portional resection showing amount of bowel removed from, and remaining in, a 3-week-old puppy weighing 0.9 kg.
B, Following completion of end-to-end anastomosis in two layers with 000000 silk.

type of resection was started 3 in. distal to the ligament of Treitz; the ileal type of resection was ended 3 in. proximal to the cecum; and in performing a mid-portional resection, an attempt was made to leave an equal amount of proximal jejunum and terminal ileum.

The puppies were operated upon between the ages of 1 and 4 weeks at which time they weighed from 0.5 to 2.0 kg. On the day of surgery the animals were separated from the mother four hours prior to the time of operation. Open drop ether anesthesia was used routinely and proved satisfactory. The animals were placed on a warm water bag, shaved, and the skin prepared with tincture of Zephiran Chloride. The abdomen was entered through a midline incision. The small bowel from the ligament of Treitz to the cecum was delivered from the peritoneal cavity onto warm saline packs. After the necessary measurements had been obtained, the area and amount of the small bowel to be resected were determined. The mesenteric vessels to be sacrificed were individually ligated with 0000 black silk, and the bowel was divided at the appropriate levels.

Following resection, the continuity of the bowel was restored either by a two-layer end-to-end or by a side-to-side anastomosis using 000000 black silk (Fig. 1). After approximation of the mesenteric defect, the abdominal wound was closed in two layers with fine silk. The animal was returned to its litter as soon as recovery from the anesthesia was complete.

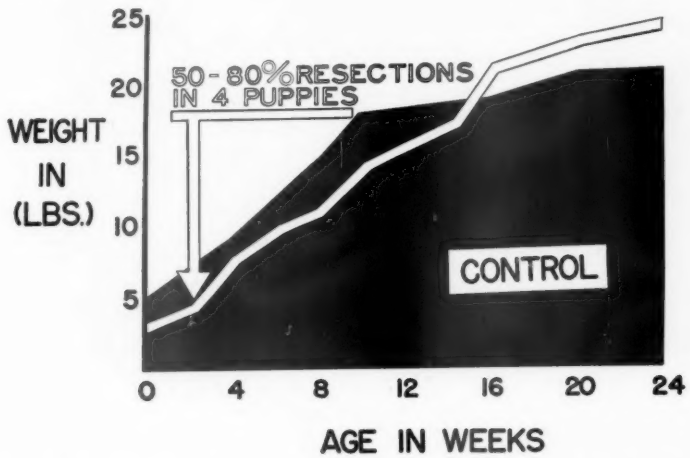


Fig. 2.—Median weight curve of four long-term litter mate animals with 50 to 80 per cent resections compared with control dog.

The puppies were nursed on an average of five weeks and were forced to complete with litter mates for their nutrients. At weaning time the animals were first offered whole milk three times daily. Later, the milk feedings were gradually fortified with commercial canned dog food until the maximum kennel diet was reached. Eventually the animals were fed only twice daily, each feeding consisting of approximately 240 Gm. of horse meat (canned dog food), 240 c.c. of fresh cow's milk, and all the whole-wheat bread each could devour. All animals received supplemental multivitamins daily.

In the early phase of this work the animals were housed in the surgical laboratory. It soon became apparent that the young animals were highly susceptible to, and frequently infected with, respiratory and enteric diseases prevalent in adult dog kennels. The major obstacle to survival was not the surgery or its effects on nutrition of the animals, but rather intercurrent diseases. For

this reason the majority of the animals were raised on a near-by farm in a kennel with the bitch. This provided space for exercise and furnished the growing puppies with a satisfactory environment. All the animals received anti-distemper immunizations and vermifuges at appropriate periodic intervals.

RESULTS

Nineteen of the twenty-five animals studied underwent extensive resections of the small bowel, while six were retained as controls.

Of the nineteen operated upon, seven animals are currently alive and have been classified as long-term survivors. One was subjected to 40 per cent resection twelve months ago; four to 50 and 80 per cent resection seven months ago; and two had a 50 per cent resection four months ago. These animals thus provide a colony of growing dogs with a median resection of 60 per cent of the small bowel that has survived an average of seven months.

Fig. 3.—Family of four long-term dogs seven months after intestinal resection. From left to right: 70 per cent jejunal resection, 65 per cent jejunal resection, 50 per cent mid-portional resection, and 80 per cent ileal resection. Weights at operation, 0.9 to 2.0 kg. Present weights, 10.5 to 11.4 kg.

The twelve remaining animals operated upon for this study survived ten to fifteen weeks and have been classified as short-term survivors. Prior to the acute episodes which precipitated their deaths, the progress of these animals compared favorably with the litter mate controls and also with the long-term survivors. Subsequent deaths in this group were attributed to the following causes: five from massive adhesions with intestinal obstruction, five from distemper complicated by intussusception, and two from injury inflicted by older, unrelated dogs. Interestingly enough, two of the control dogs also succumbed to distemper and intussusception.

The effects of such extensive resections of the small bowel on the growing animals were carefully evaluated by daily weight records as well as frequent observations of the animals' appetite, activity, temperament, and bowel habits.

Many of the animals lost weight during the first four to five days after surgery, but then resumed normal growth rates comparable to, and in some

instances greater than, the controls (Fig. 2). This occurred irrespective of the type of resection, per cent of resection, or type of anastomoses employed. The long-term survivors now range in weight from 9.6 to 12.3 kg. compared to 10.0 kg. for the control (Fig. 3).

Within a few days following the operation the appetite, activity, and the temperament of the animals returned to normal and remained so. Diarrhea, while present initially, did not appear to be a troublesome factor, and all long-term survivors are now having formed stools.

In five of the long-term survivors laboratory studies were performed in order to evaluate certain pertinent facts relative to nutrition. Monthly peripheral blood analyses revealed no significant abnormality. The red blood counts varied from 3.99 to 4.8 million compared to 3.99 million for the controls. The hemoglobin varied from 11.4 to 14.3 Gm. per cent compared to 11.4 Gm. per cent for the controls. The hematocrit values ranged from 34 to 40 per cent, the control value being 38 per cent. Thin smears of the peripheral blood revealed no evidence of macrocytosis, poikilocytosis, anisocytosis, hyperchromia, or hypochromia. Bone marrow studies revealed no significant changes. Total protein, serum calcium and serum chloride, and blood volume determinations were also constant when compared with the results of the control litter mate. Protein values, by the photometric method of Greenberg, varied from 6.0 to 7.1 Gm. per cent, compared to the control of 7.1 Gm. per cent. Serum calcium values, by the titration method of Tisdall, varied from 12.6 to 14.2 mg. per cent compared to the control of 13.2 mg. per cent. The serum chloride values, by the titration method of Schales and Schales, ranged from 100.4 to 111.7 meq., the control being 110.1 meq. Blood volume determinations performed at University Hospital, using radioactive iodinated human serum albumin, varied from 315 to 347 c.c. The control measured 342.1 c.c. (Table I).

TABLE I

LONG-TERM DOGS	40% JEJUNAL	50% MID-PORTIONAL	65% JEJUNAL	70% JEJUNAL	80% ILEAL	CONTROL
Operation						
Age (wk.)	3.0	1.0	1.5	2.0	3.0	---
Wt. (kg.)	1.8	0.9	2.0	1.1	1.6	1.1
Postoperative						
Age (wk.)	52	30	30	30	30	26
Wt. (kg.)	11.4	10.5	11.4	11.4	10.9	10.0
Length of bowel found at re-exploration (cm.)	165	125	115	79	48	255
Laboratory Analyses 26 Weeks Postoperative						
Red blood count (millions)	4.80	4.74	4.15	4.76	4.50	3.99
Hemoglobin (Gm. %)	14.3	12.0	13.5	12.7	14.2	11.4
Hematocrit (Wintrobe %)	40.0	38.0	34.0	38.0	40.0	38.0
Total protein (Gm. %)	6.8	6.2	6.4	6.5	6.0	7.1
Serum calcium (meq./L.)	13.1	14.2	13.0	13.6	12.6	13.2
Serum chloride (mg. %)	106.1	106.9	100.4	111.7	111.7	110.0
Blood volume (c.c.)	342.6	347.0	315.0	347.0	318.9	342.1

Fig. 4.—*A*, Barium x-ray studies on control animal.

B, Forty per cent mid-portional resection with end-to-end anastomosis. The anastomosis is not visible. There is little change in caliber or motility of bowel.

C, Sixty per cent jejunal resection showing somewhat dilated, but functionally satisfactory, side-to-side anastomosis. The caliber of bowel is definitely increased.

D, Eighty per cent ileal resection showing marked hypertrophy of bowel with little apparent increase in length. The motility is markedly diminished. Stomach-to-cecum barium transit time 1 to 3 hours in each animal.

Repeated x-ray studies of the gastrointestinal tract were carried out,* using an isotonic saline barium suspension for the studies (Fig. 4). The stomach showed no abnormality of contour or motility. The small intestine was increased in diameter in proportion to the percentage of the resection. In dogs with 50

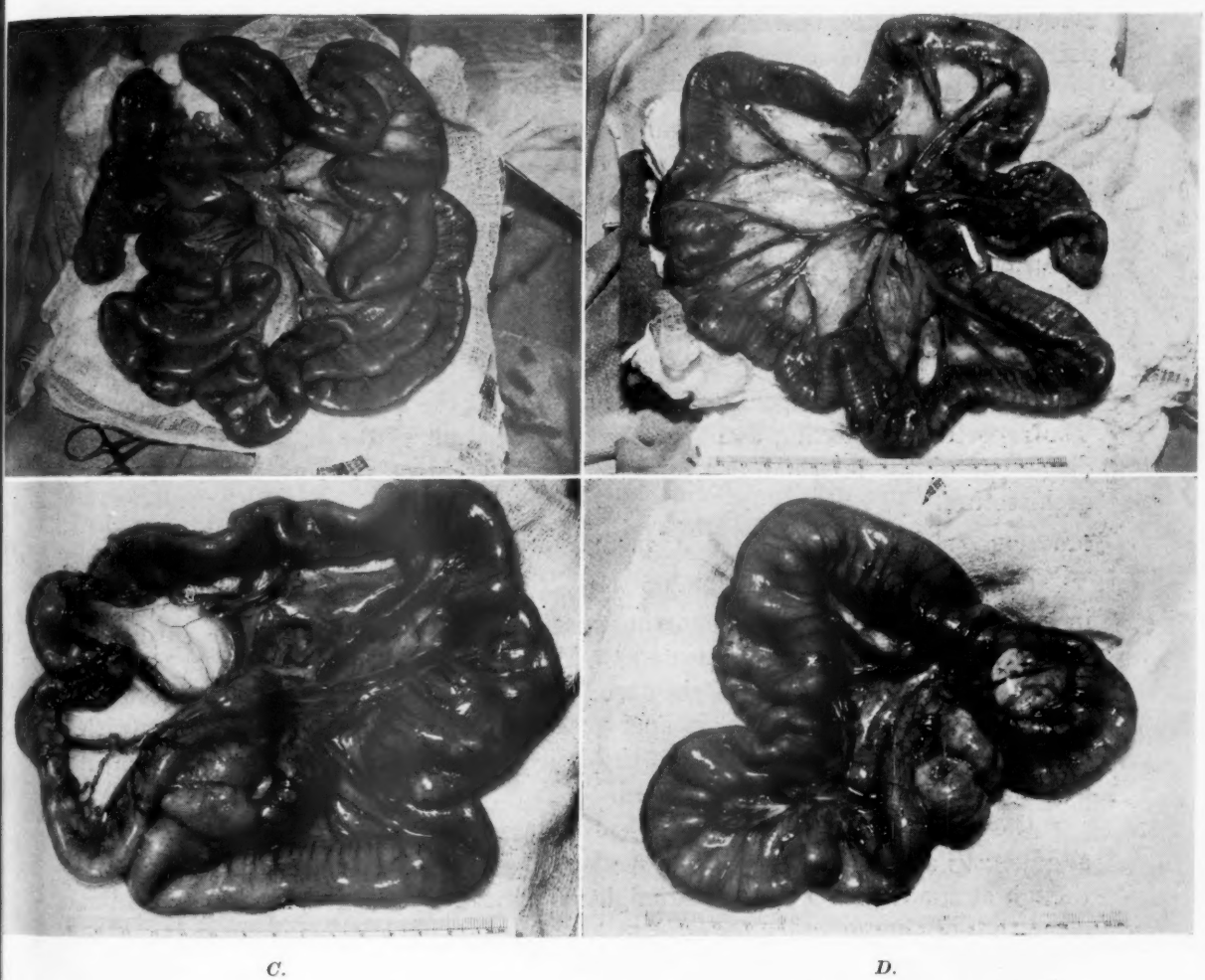


Fig. 5.—Appearance of the remaining small bowel found at re-exploration of long-term dogs shown in Fig. 3.

A, Control dog in which the small bowel measured 255 cm. from ligament of Treitz to ileocecal valve.

B, Forty per cent jejunal resection with 165 cm. remaining.

C, Sixty-five per cent jejunal resection with 115 cm. remaining.

D, Eighty per cent ileal resection with 48 cm. remaining. (Note tail of pancreas visible just proximal to ligament of Treitz.)

to 80 per cent resection the diameter of the bowel appeared to be one and one-half to two times that of the bowel in the control animals. The colon was unremarkable. The end-to-end anastomoses were not discernible and although the side-to-side anastomoses were dilated to about three times the size of the adjacent

*By Dr. Joseph L. Morton of the Department of Radiology.

intestine, there did not appear to be any interference with its function. The stomach-to-cecum transit time of the barium suspension was the same in the controls and in the operated animals, regardless of the amount resected, and varied from one to three hours. No definite evidence of nutritional deficiency was observed in the intestinal pattern. Further roentgen studies of the long bones and epiphyses of the extremities of these animals revealed no conclusive evidence of rachitic, scorbutic, osteoporotic or other changes indicative of impaired bone metabolism.

Surgical re-exploration was carried out in five long-term survivors and was tolerated well by each. The remaining small bowel in these animals was found to be increased in diameter. The length did not appear to be proportionately increased. The bowel wall was definitely thickened. In each instance, the length of the remaining small bowel was again measured and varied from 48 cm. in an 80 per cent resection to 165 cm. in a 40 per cent resection as compared with 255 cm. in the control animal (Fig. 5).

Generous biopsy specimens of the liver and of the bowel, both proximal and distal to the anastomosis, were obtained at the time of re-exploration. Histopathologic studies were performed by members of the Department of Pathology, who reported a widening and increased arborization of the intestinal villi with deepening of the lateral indentations. The liver biopsies showed normal liver architecture.

DISCUSSION

Clinical case reports involving extensive resections of the small intestine in infants and children, and reporting successful results, are rare. Of 257 cases, comprising all age groups, collected by Haymond[5] in 1935, only three massive resections were performed in children. Ruggi was credited with the removal of 330 cm. of the small bowel in an 8-year-old boy, with survival, Blayney with a 253 cm. resection in a 10-year-old child, and Jackson[6] with 142 cm. of ileum in a 24-month-old infant who recovered.

General surgeons widely experienced in pediatric surgical problems[4] have assiduously avoided the massive resection of small bowel in the very young, although at times such a procedure might offer not only the simplest approach but often the only opportunity for cure.

The few previously recorded experimental studies tend to substantiate this general pattern of reserved judgment. As early as 1912 Flint[3] notes that young dogs do not tolerate extensive intestinal resections as well as older animals. In 1942 Petri[7] resected the distal small bowel in three 5-month-old, 5.7 to 7.8 kg., dogs, removing an estimated 81, 63, and 60 per cent of the entire jejunum and ileum in an effort to produce a macrocytic anemia. According to his protocols these animals succumbed to nutritional deficiencies 82 days, 140 days, and 146 days later. During life, inhibition of growth, loss of appetite, emaciation, and diarrhea were noted three weeks postoperatively. Each developed first a hypochromic, then a macrocytic type of anemia.

In contrast with these observations, the animals used in our study were somewhat younger than those employed by Petri. Yet our long-term survivors

with comparable resections evidenced none of the extreme metabolic or hematopoietic abnormalities noted by him. On the contrary, our young dogs tolerated the massive resections as well as, or better than, adult animals.

The mechanism of compensation presents an intriguing problem in itself. As previously described by Flint, our animals also developed hypertrophic changes in the intestinal villi and an increased caliber of the bowel itself. In addition, fluoroscopic studies revealed a definite change in intestinal motility, since the stomach-to-cecum transport time was similar regardless of the length of the small bowel present. Together these gross changes would result in prolonged contact of the succus entericus with an enlarged mucosal surface area possessing markedly modified and more effective intestinal villi. What other biophysical alterations may contribute to this remarkable compensatory state are as yet unknown.

Irrespective of the mechanism of compensation, these experimental observations made on growing dogs suggest that massive small bowel resection be considered a reasonable venture in very young clinical patients. In infants and children where congenital anomalies or neoplasia clearly indicate the removal of 40 upward to 80 per cent of the small bowel to insure eradication of the disease, the surgeon may proceed with reasonable assurance that the subsequent growth and development of the child will not be seriously impaired.

CONCLUSIONS

1. Forty to eighty per cent of the small intestine distal to the ligament of Treitz has been resected in nineteen puppies without impairment of their growth and development.

2. The mechanism of compensation is apparently dependent upon an increase in absorptive surface and a decrease in the motility of the remaining small bowel.

3. These experimental observations suggest that massive resections of the small intestine may also be successful in infants and growing children.

Acknowledgment.—We acknowledge with gratitude the invaluable aid afforded us by Mr. Judah Folkman who enthusiastically assisted with the operations, anesthesias, and the care of the animals.

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DISCUSSION

DR. HOWARD ULFELDER.—I enjoyed very much Dr. Clatworthy's presentation. It gives me a little hope that a patient whose case I am following at the moment may not end in quite so bad a condition as I had feared she would. This patient was brought into our hospital just about two years ago, at the age of 3 days, with a history that nothing had passed by rectum since birth. There was moderate abdominal distention. The patient weighed 4 pounds and 14 ounces. Diagnosis of complete small bowel obstruction was made and the following roentgenograms were taken (slides): The one on the left illustrates, I think, very clearly to you the dilated small bowel, and the one on your right is a barium enema which we interpreted erroneously since large bowel was demonstrated only on the left side of the abdomen, although it seemed rather long and coiled. We operated on this patient and we discovered that these roentgenograms actually illustrate all of the intestinal tract that is useful in this infant. She had complete atresia of the small bowel from a point about three loops below Treitz's ligament down to the ileocecal valve which lay in the left upper quadrant. A side-to-side anastomosis was performed between the dilated bulbous end of small bowel and the cecum. I went to the trouble of resecting all of the bowel that was atretic because it contained numerous short dilatations that looked very much like a string of beads on the edge of the mesentery. This patient survived, and she is now a little less than 2 years old. She has had a rather hard time of it, suffering intractable diarrhea for a long time. Transit time by carmine given by mouth was less than an hour at first and is now about 2 or 2½ hours. This lantern slide shows a barium meal given to the patient at the age of 1 year and you will see there the stomach outlined very well. Here we see several loops of what look like normal small bowel, although the roentgenologist interpreted them as being somewhat dilated and hypertrophied, and some barium already in the large bowel which has now expanded to fill almost the entire abdominal cavity, with the free sigmoid loop, as I interpret it, lying practically over in the right upper quadrant. This slide will illustrate this patient's progress to you in the form of graphs. As you see, on the left-hand side, she is below normal weight and has always been so. She is below normal height and has always been so. She has just been in the hospital for a very thorough study and, actually, by our laboratory tests, we can demonstrate only two deficiencies in this patient. She is constantly anemic with a level of hemoglobin of about 9 Gm., and she is abnormal in her protein with a low serum albumin. This patient, of course, has not developed quite normally as far as walking and behavior are concerned, although she seems bright and alert. It has constantly been my fear that this girl will not make it. But, as far as I can tell from the course in the last year, she is not losing ground. I want to thank Dr. Clatworthy again. He has given me some hope.

DR. ROBERT E. GROSS.—These investigators have put their finger on a very important problem because so many of us have encountered this question of extensive removal of intestines in small babies. We certainly go along with the authors in believing that 50 or 60 per cent of the intestine can be removed and still have an individual who can survive and enjoy good health. This has been done in human beings on a number of occasions. But there are those situations where one is driven to an 80 or 90 per cent resection, and it has been our experience that in this range the outlook is very poor. We have had three patients who have been subjected to such removals. One died in a few weeks; one died at two months; one went nearly ten months before increasing inanition finally led to death.

I believe one can have selective deficiencies after extensive resections. We saw this in one boy with massive resection who was reasonably well, as far as his general nutritional state was concerned, but who had difficulty in absorbing fats. A low vitamin D uptake led to a deficiency of calcium absorption and finally produced a hemorrhagic diathesis.

DR. CLARENCE DENNIS.—The question naturally arises when one is discussing such a situation as this, whether or not the colon may take over a fair share of the absorptive function of the intestine that has been removed. I would like to point out one case in which it seems to me this was pretty well ruled out. I did an ileostomy on a girl in 1941, at which time

she was 13 years of age. With one complication or another, primarily ascending enteritis, extending from the ulcerative colitis from which she was suffering in the first place, she, for the past four and a half or five years, has had but 5½ ft., measured, of small intestine from the ligament of Treitz to her ileostomy. The rest of her small intestine has been removed. The colon and rectum have also been removed, as well as a gangrenous gall bladder. She maintains a very satisfactory state of nutrition at the present time. If the weather gets hot, or if she gets a respiratory infection, she has trouble with water and salt balance problems, as you might imagine. However, her serum protein level remains in a good solid normal range. Her appetite is excellent at the present time, and her hemoglobin stays where it belongs. It seems as though she has gradually acquired, as the years have gone by, a better ability to sustain herself. There is some compensation, which I am sure none of us taking care of her understands. It has been studied rather carefully, but we don't know quite what happened. She keeps her hemoglobin up better now than she did four or five years ago and she keeps her serum protein normal, which she did not four or five years ago.

DR. EDGAR J. POTH.—I should like to comment on this interesting paper by recounting briefly the results of massive resections of small bowel in two children and one infant.

One child, now twelve years of age, has had severe gastrointestinal hemorrhages since birth, requiring massive transfusions at increasingly frequent intervals until it has become impractical to so maintain the circulation. A laparotomy ten years previously had resulted in the diagnosis of hemangiomas involving the entire small bowel. Reoperation recently demonstrated vascular anomalies involving the jejunum and ileum extending from 45 cm. from Treitz's ligament to a point on the ileum 75 cm. proximal to the ileocecal valve. Two hundred ten centimeters of jejunum and ileum were resected. Postoperatively, there was no diarrhea or other gastrointestinal disturbances and the child has progressively gained weight on an ordinary diet.

The second child, now eleven years of age, had had an exclusion operation of an estimated two-thirds of the small bowel at five years of age. The atrophic-excluded segment measuring 120 cm. in length and 2 cm. in circumference was excised recently. At the age of 11 years this child weighed 54 pounds.

An infant 39 hours of age was explored because of intestinal obstruction. Atresia of the entire colon and volvulus of the distal ileum, with necrosis involving essentially the entire ileum, was found at operation. The ileum was resected and the distal end of the small bowel was brought out as enterostomy. There has been a severe postoperative electrolytic imbalance. The child is alive four weeks after operation, and the prognosis is fair.

DR. CLATWORTHY (Closing).—I want to thank all of the discussers, particularly those who have added some information on the clinical side to go with these brief experimental observations. We are distinctly concerned about resections over 80 per cent. I personally had the feeling that our dog with 80 per cent resection was right at the upper limit and that we would anticipate difficulties beyond it. I think it is extremely important, from the clinical side, to have these arcades counted, if possible, and the remaining bowel measured in youngsters who are subjected to this procedure. In any instance, we feel that an extensive resection of the small intestine should not be avoided simply because the patient is an infant.

CONGENITAL MALFORMATIONS OF THE RECTUM AND ANUS

I. Clinical Features and Surgical Management in 120 Cases

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THE literature pertaining to congenital malformations of the rectum and anus constitutes a far from brilliant page in the history of surgical endeavor. The immediate mortality, the limited number of long-term survivals, and the otherwise unhappy results pose a difficult challenge to surgical progress in this field. The physicians of classical antiquity regarded anal imperforation as an incurable monstrosity. The first mention of an attempt at surgical intervention is to be found in the writings of the Byzantine physician, Paul of Aegina (625-690 A.D.). He advocated the blind plunge of a knife into the perineum in the hope of entering the rectal pouch. This primitive approach, later supplemented by repeated postincisional dilatations, remained the accepted treatment for centuries, varying only with respect to the length, depth, and angle of the perineal incision.

The most significant early contribution* to the surgical management of anorectal anomalies was made in 1835 by Amussat.[1] He introduced the technique of perineal anoplasty and emphasized the importance of careful perineal dissection in the identification and mobilization of the rectal pouch so that the rectal mucosa could be sutured to the skin edges without tension. It was soon discovered, however, that the blind end of the rectal pouch was too high, in occasional cases, to be reached by simple perineal exploration. Some surgeons advised colostomy in cases of perineal failure, while others resorted to more radical perineal operations including parasacral dissection, coccygeal or sacral resection, and sacral splitting procedures,[4, 10, 21, 22] An excellent historical review of the development of the operative techniques for imperforate anus was presented before the American Surgical Association by Rudolph Matas,[13] in 1897.

Lost in the general enthusiasm for perineal anoplasty were the worth-while suggestions of MacLeod,[12] in 1880, and Delageniere,[5] in 1894, concerning the merits of combined abdominoperineal anoplasty. In cases of perineal failure, MacLeod recommended laparotomy to identify the high rectal pouch and suggested the combined use of both wounds to effect a pull-through of the distal hindgut for perineal suture. Delageniere advocated initial abdominal exploration with subsequent utilization of a perineal incision for pull-through following transabdominal identification of the blind end of the rectal pouch. Interest in the simultaneous abdominal and perineal approach was revived with the

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*The contribution of Amussat was directed primarily toward anorectal reconstruction. It should be noted that imperforate anus has also played an important role in the early development of colostomy, from Littré to Duret. For further details, the reader is referred to the scholarly work of Tilson Dinnick (The Origins and Evolution of Colostomy, Brit. J. Surg. 22: 142, 1934).

report, in 1948, of 2 cases by Rhoads, Pipes, and Randall.[20] They advised the combined approach when it was apparent that the rectal pouch could not be safely reached from below. Further experience with this method has been published by Norris, Brophy, and Brayton.[18]

Although the literature concerning anorectal anomalies abounds in reports of isolated cases, the number of large series reported is small. We have encountered only 2 series in excess of 100 cases,[9, 14] and only 3 others in excess of 50 cases.[2, 11, 18] It has, accordingly, been felt desirable to report the experience at this institution with 120 cases of congenital malformations of the rectum and anus during a 25 year period (1926 to 1951). We also wish to present an evaluation of the results in 11 patients upon whom abdominoperineal anoplasty has been carried out during the past 3 years. Twenty-three of the cases included in this study have been previously reported by Berman in 1938.[3]

INCIDENCE

Sixty-nine of the patients in this series were male (58 per cent) and 51 were female. Some question existed as to the sex in 4 of them. Two were regarded as probably male and 2 as probably female. Three of the patients were Negro infants, while 117 were white.

Anorectal malformations have been estimated to occur approximately once in every 5,000 births.[6, 9] Six infants with imperforate anus were born at this medical center during the period covered by this study. During the same period there were 26,736 births, an incidence of approximately 1 in 4,500 births. A family history of imperforate anus was encountered in only 1 of the 120 cases.

The average number of new cases seen each year has steadily increased during the period of this survey (Table I). The presence of 10 new and old cases on the wards of this hospital at one time during the past year emphasized to us the need for the current analysis.

TABLE I. AVERAGE NUMBER OF NEW CASES OF ANORECTAL ANOMALIES SEEN PER YEAR

PERIOD	1926-29	1930-34	1935-39	1940-44	1945-49	1950-51
Average no. cases	1.8	2.8	3.2	4.8	8.0	9.5

TYPES OF MALFORMATION

Ladd and Gross[8] have divided anomalies of the rectum and anus into 4 clinical types (Fig. 1). The malformation in Type 1 consists of a stenotic narrowing of the rectum or anus, the hindgut being otherwise patent. In Type 2, the rectal pouch is low, whereas in Type 3 it is somewhat higher, with several centimeters often separating it from the skin of the perineum. There is an atresia of the rectum in Type 4, the anus and lower rectum appearing normal. Five of the cases in this series were classified as Type 1, 20 as Type 2, 90 as Type 3, and 5 as Type 4 (Table II).

A congenital fistulous communication existed between the blind end of the hindgut and the bladder, urethra, perineum, or vagina in 70 of the 120 patients (58 per cent). The fistulas were predominantly into the urinary tract

in male patients and into the vagina in female patients (Table III). Multiple fistulas occurred in only 2 instances. One male infant had both rectovesical and rectoperineal fistulas and 1 female infant had both rectovaginal and rectoperineal fistulas. In 2 cases, a rectovesical fistula opened onto an extrophy of the bladder and, in another case, a rectovaginal fistula entered a hydrometrocolpos. An understanding of the embryologic development of the hindgut and the urogenital tract facilitates a clearer visualization of the manner in which these anomalies probably occur. Excellent, detailed descriptions of the embryology of this region have been published by Ladd and Gross[8] and Berman.[3]

TABLE II. DISTRIBUTION OF PATIENTS ACCORDING TO TYPE OF MALFORMATION

TYPE	WITHOUT FISTULA			WITH FISTULA			TOTALS
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL	
1	3	2	5	0	0	0	5
2	12	3	15	2	3	5	20
3	20	6	26	29	35	64	90
4	3	1	4	0	1	1	5
Total	38	12	50	31	39	70	120

TABLE III. DISTRIBUTION OF FISTULAS

TYPE OF FISTULA	MALE	FEMALE	TOTAL
Rectovesical	13*	1	14
Rectourethral	11	0	11
Rectoperineal	7	9	16
Rectovaginal	0	29†	29
Total	31	39	70

*One infant had both rectovesical and rectoperineal fistulas.
†One infant had both rectovaginal and rectoperineal fistulas.

CLINICAL FEATURES

The basic picture in untreated cases of anal or rectal imperforation, without adequate fistulous decompression, is one of progressive low colonic obstruction with abdominal distention and vomiting. Death ultimately occurs from colonic rupture, loss of fluids and electrolytes or tracheobronchial aspiration of vomitus.

The diagnosis of anal imperforation is readily made in Type 2 and 3 cases by inspection of the perineum. Careful digital examination of the anus and rectum is necessary, however, to establish the cause of the patient's obstructive symptoms in Types 1 and 4. The method of roentgenologic examination of the infant in an inverted position with a metallic marker in the anal area, as described by Wangensteen and Rice,[23] is of great help in determining the position of the blind rectal pouch in relation to the anus. The accuracy of this examination is increased if the radiologic study is carried out after the first 24 hours following birth.

The existence of vaginal or perineal fistulas may be suspected from a history of the passage of meconium from the vagina or an abnormally placed "anus." It may be confirmed by local examination. Rectoperineal fistulas generally occur in the midline of the perineum and may even, in rare instances, open onto the ventral surface of the penis simulating a duplication of the ure-

thra.[7] The insertion of a curved hemostat or probe into rectovaginal or rectoperineal fistulas with simultaneous digital palpation in the anal area may elicit valuable information concerning the location of the rectal pouch. Roentgenographic studies, following lipiodol injection into the fistulous tract, may also be helpful.

The demonstration of urinary tract fistulas is considerably more difficult and many of them, unfortunately, are overlooked, especially when the operative approach is solely perineal. The passage of air or meconium through the urethra on urination and the presence of air bubbles in the bladder upon radiographic examination are strong presumptive evidence of a fistulous communication. Roentgenologic visualization of a fistula can occasionally be obtained following the instillation of a radiopaque media into the bladder. Still, it appears that the most reliable method identifying, as well as closing, urinary tract fistulas is by means of the combined abdominal and perineal operation.

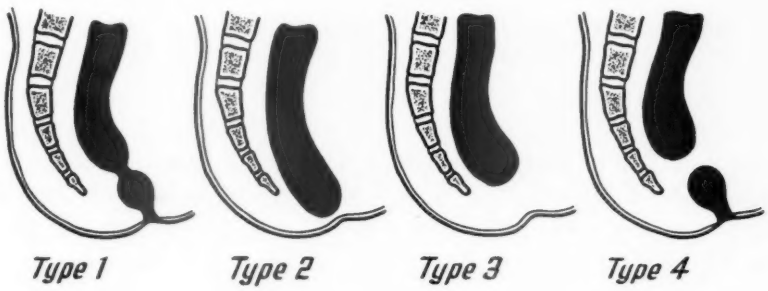

Fig. 1.—Ladd and Gross classification of clinical types of anorectal malformation (redrawn from Ladd and Gross[9]).

Infants of Type 1 are generally not seen as early in life as are the patients of other groups. They most often suffer from progressive constipation with frequent fecal impactions and the passage of ribbonlike stools. Type 2 and 3 patients, without adequate fistulous decompression, are most often referred to the hospital during the first hours or days of life. Of all the patients with complete obstruction, the diagnosis is most frequently delayed in Type 4 cases, contributing to the higher mortality in this group. Patients with vaginal or perineal fistulas may, occasionally, go for months or even years without serious difficulties beyond the need for periodic dilatations, enemas, and fecal disimpaction.

Additional congenital anomalies were encountered in 86 of the 120 patients (72 per cent) and in 33 of the 34 patients upon whom careful post-mortem studies were carried out (97 per cent). This important aspect of the imperforate anus problem will be dealt with in greater detail elsewhere.[17]

TREATMENT AND RESULTS

The careful and precise classification of anorectal anomalies according to clinical types is of great importance in planning their surgical management. The method of treatment, as well as the prognosis for both mortality and excellence of local results, varies considerably in the 4 types. For this reason,

we shall consider the experience with each type separately. Due to the high nonsurgical mortality, the presentation of operative mortality only tends to give a misleading picture of the true gravity of the imperforate anus problem. We have, accordingly, included all deaths regardless of the cause or the duration of time following operation. The technique of perineal anoplasty used in this series has been essentially that originally described by Amussat and the method of abdominoperineal anoplasty with initial abdominal incision has been similar to that advocated by Delageniere and, more recently, employed by Rhoads, Pipes, and Randall, and Norris, Brophy, and Brayton. Repeated postoperative anal dilatations have been utilized following both types of operation to prevent stricture formation at the suture line.

Type 1.—Repeated rectal dilatation was utilized as the treatment of choice in all 5 of the patients in this group. One patient died at 3 weeks of age of septicemia. Another infant developed a functional intestinal obstruction at the splenic flexure at 9 months of age for which a number of unsuccessful operative procedures were undertaken. The child is still living at 6 years of age with a permanent colostomy. The other 3 patients have responded satisfactorily to repeated dilatations and are now having normal bowel movements.

Type 2.—One of the 20 infants of this type was stillborn and 2 have died: 1 at 8 months of age during operation for subdural hematoma and 1 at 2 years of septicemia and infectious diarrhea. The operative treatment in this group consisted of excision of the anal membrane with perineal anoplasty followed by repeated dilatations. Fistulas, when present, were closed. Recent follow-up questionnaires and clinical examinations have shown the results in the great majority of the surviving patients to be excellent. Fourteen children, ranging from 6 months to 13 years of age, are now having normal bowel movements with good anal sphincter tone. The results have been less satisfactory in 3 cases. One patient is having difficulty at 3 years of age with megacolon and megaloureters. Another, an 8-year-old microcephalic child with vertebral anomalies, has had persistent constipation and only fair control of bowel movements. The third patient, a 5-month-old infant, has progressive hydrocephalus with frequent convulsions. The over-all mortality in this group has been 15 per cent.

Type 3 (Without Fistula).—Of the 26 patients in this group, 5 infants arrived at the hospital in a hopeless condition, principally because of associated anomalies, and no attempt was made toward surgical correction. All 5 infants died. No effort at anorectal reconstruction was made in 5 patients who had been given colostomies elsewhere. Two previous unsuccessful attempts at perineal anoplasty had been made on 1 of them. One of these infants died at 4 months of age of diarrhea. Colostomy was carried out on 2 infants at this hospital. Both infants died of additional congenital anomalies, 1 at 1 day and 1 at 3 months following operation. Perineal anoplasty was performed in 11 cases. Nine of these patients have died from 1 day to 2 years following operation, in most cases from associated congenital malformations or infections. Two patients have survived 9 and 12 years following perineal anoplasty. Both are partially incontinent of feces and have no demonstrable anal sphincter action.

They are otherwise healthy and active. Combined abdominoperineal anoplasty has recently been carried out in 3 cases without mortality. Seventeen of the 26 patients in this group have died, a mortality of 65 per cent.

Type 3 (Male Child With Fistula).—No attempt was made at surgical intervention in 4 of the 29 patients in this group because of the serious nature of the associated anomalies. All 4 patients died. Colostomy at birth had been carried out elsewhere on 2 patients; 1 died in this hospital of renal failure at the age of 14 months and the other has had a perineal anoplasty elsewhere and is living at 6 years of age, but has no control of his bowel movements. Perineal anoplasty had been performed elsewhere on 4 patients. All 4 of these patients still had urinary tract fistulas when first seen at this hospital and the anal reconstruction was unsatisfactory in all of them. One died of other anomalies at 10 weeks of age and 1 died elsewhere at 8 years. The oldest is still living at 28 years of age, although in poor health.

Death from unrelieved intestinal obstruction occurred in 1 case following an unsuccessful attempt at perineal anoplasty at this hospital. Colostomy was carried out on 4 patients and 2 have died. One of the living patients has subsequently had a perineal anoplasty elsewhere and is incontinent of both urine and feces at 6 years of age.

Eight of the patients in this group were treated in this hospital by primary perineal anoplasty. Four have died from 1 day to 2 months following operation and 2 have been lost to follow-up since discharge from the hospital. Neither of the other 2 patients has control of bowel movements. One of them still has a urinary tract fistula and the other child is mentally retarded. Combined abdominoperineal anoplasty was carried out in 6 cases with no operative deaths, although 2 infants have died during subsequent hospital admissions at 3 and 14 months of age. Death has occurred in 16 of the 29 cases in this group, a mortality of 55 per cent.

Type 3 (Female Child With Fistula).—Ten of the 34 patients in this category have been treated by local measures, principally by dilatation of fistulas, without operation. Six of these patients have died between 1 day and 6 months of age, 5 of other anomalies and 1 of diarrhea. One patient, whose only treatment has been repeated dilatations of a rectoperineal fistula, has been followed for 19 years and is now able, with the aid of careful dietary regulation, to control her bowel movements.

Colostomy was performed as the only operative procedure at this hospital in 2 cases without mortality; in 1 case because of intestinal obstruction secondary to inadequate rectovaginal fistulous decompression at 12 months of age and in the other because of scarring in the region of a perineal anoplasty performed elsewhere. A 22-year-old woman, who had had difficulty for years with an inadequate sigmoid loop colostomy and persistent fecal discharge from a rectovaginal fistula, was treated by an abdominal resection of a massively dilated distal hindgut segment with closure of the vaginal fistula and the creation of a permanent colostomy. A normal 9 pound infant was delivered by cesarean section from a 19-year-old woman who had had an unsuccessful perineal anoplasty elsewhere during infancy with recurrence of her vaginal fistula.

Perineal anoplasty was carried out, at this hospital, on 19 patients. There were 3 deaths: from untreated esophageal atresia at 7 days of age, lung abscess at 5 months, and intussusception at 11 months. Secondary perineal operations were performed on 3 patients, following unsuccessful primary perineal anoplasty elsewhere, and were disappointing in all 3 cases. The results in 10 cases of primary perineal anoplasty at this hospital have been unsatisfactory due to fecal incontinence, perineal scarring necessitating colostomy, fistula recurrence or loss of the rectovaginal septum. One of these patients, who was operated upon at 9 years of age, was found to have a recurrence of her vaginal fistula at the fourchette with fecal incontinence in the early postoperative period. She has been followed for 25 years and has now, at 34 years of age, gained control of bowel movements through her recurrent fistula, aided by the most careful dietary regulation and supplemented by levator and gluteal action. This patient is doing well and feels quite strongly that her current "perineal colostomy" is far more desirable than an abdominal colostomy. Another patient, followed 9 years, with no anal sphincter activity is now acquiring control of her bowel movements in a similar manner. One patient is having normal bowel movements with a good anal sphincter 9 years after operation. Sphincter activity was reported present in 2 patients on the basis of 1 year postoperative follow-up studies, but they have both unfortunately been lost to follow-up.

Two patients have recently been treated successfully by abdominoperineal anoplasty. Nine of the 35 patients in this group have died, a mortality of 26 per cent.

Type 4.—All 5 of the patients of this type have died. One patient whose obstruction had been relieved by a transverse colostomy died at 6 weeks of age from other anomalies. An attempt at perineal operation was unsuccessful in 1 case and, in another, a gangrenous, perforated small intestine, due to a constricting band around the base of a short mesentery, was found at laparotomy. Operative treatment was not attempted on the other 2 patients because of their hopeless condition on arrival at the hospital. The mortality in this group was 100 per cent.

TABLE IV. CAUSES OF DEATH

Associated anomalies	23
Bronchopneumonia	6
Infectious diarrhea	4
Intestinal obstruction	3
Septicemia	3
Peritonitis	3
Shock	2
Idiopathic hemorrhage	1
Urinary tract infection	1
Lung abscess	1
Subdural hematoma	1
Intussusception	1
Stillborn	1
Total	50

Thus, 50 of the 120 patients in this series (42 per cent) have died, either in this hospital or elsewhere, during the period covered by this study. The longest postoperative follow-up has been 25 years and the greatest interval be-

tween operation and death has been 8 years. Although the precise cause of death was difficult to determine in several of the cases, we have attempted to evaluate as accurately as possible the principal factors leading to death (Table IV). The presence of other congenital abnormalities has accounted for the largest number of fatalities. Prematurity was a significant contributing factor in the demise of 4 of the infants who died of associated anomalies and in the case of 1 of the infants who succumbed to diarrhea. It is likely that the over-all mortality for this group of patients will rise even higher during the next few years due to the fact that the prognosis in a number of the living patients must be considered poor, primarily because of other congenital abnormalities.

Abdominoperineal Anoplasty.—In the past 3 years, abdominoperineal anoplasty has been carried out in 11 cases of Type 3 anorectal anomaly without operative mortality. However, 2 infants, operated upon at birth, have died: 1 from an episode of massive, spontaneous gastrointestinal hemorrhage during a second hospital admission at 3 months of age and 1, with serious upper urinary tract anomalies, of shock and fluid mismanagement following colostomy closure during a third hospital admission at 14 months.

Abdominoperineal anoplasty has been performed as the primary procedure at birth in 7 cases. Two patients, as has been mentioned, have died at 3 and 14 months of age. One of the 2 patients, followed over 1 year postoperatively, has a good anal orifice and a functioning anal sphincter, while the other has an adequate anal opening but without evidence of an anal sphincter. The period since operation has been too short to evaluate sphincter activity accurately in the other 3 infants. All 3 have satisfactory anal openings. A colostomy has been necessary, however, in 1 of these infants because of functional intestinal obstruction 6 weeks after operation.

Colostomy at birth, following failure to locate the rectal pouch by perineal dissection, had been utilized in 2 patients upon whom abdominoperineal anoplasty was performed at 14 months and 2½ years of age. There is no evidence of anal sphincter activity in either case, although both have otherwise adequate anal openings. Abdominoperineal anoplasty was carried out, at 17 months and 4 years of age, on 2 patients treated at birth by colostomy only. Although both have patent anal orifices without stricture or scarring 2 and 3 years after operation, no sphincter action is demonstrable in either case.

Two of the surviving patients are mentally retarded. One of these children has radiologic evidence of megacolon in the absence of anal stricture or perineal scarring. One other patient still has a colostomy which was created because of functional intestinal obstruction. The suspicion that distal colonic motility may be congenitally deficient in some patients with anorectal anomalies has led us to adopt a policy of carrying out frozen section microscopic studies for myenteric plexus ganglion cells on the terminal colonic segment before utilizing it for pull-through mucocutaneous suture.[16] Frozen section studies of terminal colon at operation on a recent patient, treated by abdominoperineal anoplasty, demonstrated the presence of normal-appearing Auerbach's ganglia. This patient has had an uncomplicated postoperative course with good bowel movements and no evidence of colonic motility difficulties.

The terminal colonic segment was doubled back upon itself in a U shape in 2 cases, with the blind end directed cephalad and secured in that position by its vascular supply. It was, thus, necessary for technical reasons in both cases to sacrifice this terminal blood supply and resect approximately 6 cm. of the terminal colon in order to obtain a colonic segment which could be satisfactorily pulled through the perineal incision for mucocutaneous suture without tension. In 1 other instance, despite a relatively low rectal pouch, division of an unimportant vascular bundle through the abdominal incision was required to obtain sufficient colonic length for perineal skin suture without tension.

Urinary tract fistulas were easily and successfully managed, by ligation and division, through the abdominal incision; rectourethral fistulas in 3 cases and rectovesical fistulas in 3 cases. Urinary tract fistulas were found to be present in 6 of the 8 males treated by abdominoperineal anoplasty. Suprapubic cystostomy was also carried out on 3 of these patients. A rectovaginal fistula was easily dissected free through the abdominal incision and ligated through a small perineal incision in a female infant operated upon at 17 days of age. In another patient, operated upon at 2 days of age, a rectovaginal fistula was both dissected free and ligated through the abdominal incision.

The most successful anal result has been achieved in a patient who has had an equally successful repair of an esophageal atresia with tracheoesophageal fistula.

Fig. 2.—Photograph showing prolapse of right colon and terminal ileum through transverse colostomy.

COMPLICATIONS

A wide variety of complications were encountered. Local difficulties associated with the operative procedure and complications resulting from delayed diagnosis and the presence of other anomalies have already been discussed. Systemic infections were troublesome in the earlier cases, before the availability of antibiotics and contemporary means of parenteral replacement therapy. Infactious diarrhea, septicemia, otitis media, meningitis, pneumonia, and pericarditis have accounted for some of the morbidity and mortality. Cystitis and pyelitis were occasionally found in the absence of demonstrable urinary tract anomalies or fistulas. Operative removal of bladder calculi was necessary in 2 cases.

A number of the patients suffered from colostomy complications. Several patients with loop colostomies developed fecal impactions in the blind distal segment of the colon, due to the incomplete diversion of fecal material. Mayo and Rice[14] have recently reported similar difficulties. The most serious difficulty, however, resulted from prolapse of the colostomy.

Prolapse, requiring operative reduction, occurred in 7 cases and, in 3 of them, the entire right colon and terminal ileum prolapsed through transverse colostomy openings onto the abdominal wall (Fig. 2). One patient experienced complete right colon prolapse on 2 occasions, 6 and 9 weeks following the original colostomy. Single prolapses took place in the other 2 cases, 4 and 9 months after colostomy. The cecum and ascending colon were mobile in all 3 and, in the most recent instance of prolapse, an attempt was made to secure the cecum in the right lower quadrant by a series of interrupted sutures of fine silk. There were 2 instances of prolapse from a distal, nonfunctioning colostomy opening.

Intussusception occurred as a complication in 3 of the Type 3 cases. One patient died at 11 months of age, of an ileocolic intussusception, at another hospital. An ileoileal intussusception was successfully reduced operatively in a 2-year-old boy, 10 days following an abdominoperineal anoplasty. The third patient, a 13-month-old boy, was treated by barium enema reduction under fluoroscopic manipulation without difficulty.[15]

DISCUSSION

Several interesting observations have been derived from this study. It appears that the designation of results, mortality-wise, in terms of length of survival is considerably more revealing than a mere consideration of operative mortality. The mortality aspects of the imperforate anus problem are, to be sure, complicated by the high incidence of associated congenital abnormalities. Many of the deaths which would have to be regarded as operative fatalities were, in fact, due more to the presence of other anomalies than to the relatively mild trauma inflicted upon the patients during the operative procedures. With safe anesthesia and proper management of fluid and electrolyte administration, otherwise healthy infants with anorectal malformations will tolerate considerable operative trauma. This fact is well illustrated by the observation that abdominoperineal anoplasty could be carried out without operative mortality in 11 consecutive cases. One infant survived both abdominoperineal anoplasty and extrapleural end-to-end esophageal anastomosis, following ligation of a tracheoesophageal fistula, carried out within a 24 hour period during the first few days of life.

The classification of each patient according to the clinical type of malformation is of great importance in determining the method of surgical management. The treatment of Type 1 patients by repeated anorectal dilatations and Type 2 patients by perineal excision of the anal membrane with perineal anoplasty has, on the whole, been quite satisfactory. The great majority of these patients are living with good anal sphincter tone and normal control of bowel movements. The failures have been due to other congenital difficulties.

The results from the management of Type 3 patients have, on the other hand, been disappointing in the majority of cases. The over-all mortality has been high (46 per cent) and functional anal sphincter activity has been rare. Unfortunately, the bulk of the cases in this series (75 per cent) were of Type 3. Many of these infants arrived at the hospital in such hopeless condition that surgery was not attempted. Furthermore, the results with perineal anoplasty have generally been poor. This operation is no longer used at this institution in the management of Type 3 anomalies. Perineal dissection had to be abandoned in 5 cases because of failure to reach the rectal pouch. Unsatisfactory results were encountered in all of the 7 patients upon whom perineal anoplasty had been carried out elsewhere and the results with secondary perineal anoplasty were poor in all of the 4 patients upon whom the procedure was attempted. Primary perineal anoplasty was performed at this hospital in 34 cases of Type 3 malformations. Sixteen patients have died and 4 have been lost to follow-up. Sphincter action was said to be present in 2 of these lost patients on the basis of short follow-up studies. The results, based on recent clinic examinations and follow-up histories, are poor in 13 of the surviving patients. Only 1 patient now has good sphincter activity and normal control of bowel movements.

The number of urinary tract fistulas overlooked in Type 3 male children, treated both here and elsewhere by perineal anoplasty, has been high in this series. Herein lies one of the more clear-cut advantages of the abdominoperineal over the perineal operation. The abdominoperineal exposure permits the identification and closure of urinary tract fistulas with relative ease. We suspect that the true incidence of urinary tract fistulas in Type 3 male children may be somewhat higher than is generally reported in the literature or was found in this series. Ladd and Gross[9] reported the presence of urinary tract fistulas in 28 of 75 Type 3 male children (37 per cent). In this series, urinary tract fistulas were discovered in 24 of 49 Type 3 male children (49 per cent). However, since abdominoperineal anoplasty has been carried out routinely on all Type 3 patients, urinary tract fistulas have been encountered in 6 of 8 Type 3 boys (75 per cent). It may also be that the disparity in the over-all incidence of congenital fistulas between Type 3 girls (85 per cent) and Type 3 boys (59 per cent) is, to a degree, more apparent than real.

The number of patients treated by the combined abdominal and perineal approach has been too small and the length of time since operation too limited to permit any rigid conclusions concerning the functional success of anorectal reconstruction, particularly with reference to anal sphincter activity. Although we remain rather pessimistic concerning the likelihood of achieving good anal sphincter action in the majority of Type 3 patients, we do feel that abdominoperineal anoplasty at birth will ultimately prove to offer the best chance for obtaining a functioning anal sphincter. The reduction in the necessary amount of perineal dissection, resulting from the use of the combined abdominal and perineal operation, both lessens the opportunity for injury to any existing and potentially functional anal sphincter muscle and minimizes the stimulus to extensive perineal scar formation. Furthermore, the more adequate mobilization

of the terminal colonic segment through the abdominal incision permits mucocutaneous approximation under less tension. The uniformly poor results from secondary anoplasty suggest that the greatest chance for success lies with the initial attempt. The experience with delayed anoplasty has also proved disappointing.

The unhappy experience of not infrequently discovering the rectal pouch to be too high to be reached by perineal dissection is easily avoided by the use of abdominoperineal anoplasty. The resection of a segment of terminal colon for technical reasons, as was necessary in 2 cases, could obviously be carried out only through an abdominal incision.

The ease with which rectovaginal fistulas may be managed with the combined abdominal and perineal approach suggests that the use of this procedure may be helpful in reducing the incidence of recurrence of rectovaginal fistulas. Gentle abdominal exploration through the abdominal incision may lead to the discovery of other congenital abnormalities which might otherwise have been overlooked, particularly in genitourinary and gastrointestinal tracts. A few of these additional anomalies may require operative treatment.

The incidence of severe constipation, sluggish bowel movements, recurrent fecal impactions, and functional intestinal obstruction in this series has been considerably greater than could be accounted for solely by the mechanical obstruction of perineal scarring or stricture at the mucocutaneous suture line. Our initial studies suggest that a deficiency in the motility of the distal colon, possibly congenital, may be, at least partially, the explanation of this difficulty in some cases.[16] Frozen section microscopic studies for Auerbach's ganglia are routinely being carried out on the terminal colonic segment, during abdominoperineal anoplasty, prior to using it for pull-through mucocutaneous suture. This procedure adds little to the risk of operation and may prove to be a valuable safeguard. In cases in which no ganglion cells are found, it may be advisable to resect a portion of the distal colon using a more proximal segment for anal suture.

The experience with abdominal colostomy in this series has not been altogether satisfactory. The complications, both with respect to distal loop fecal impactions and proximal loop prolapse, have been, at times, quite troublesome. This observation, as well as the long-term experience with increasing control of bowel movements in several patients having either no anal sphincter or recurrent fistulas, casts some doubt on the often accepted superiority of abdominal over perineal colostomy in these patients. In an effort to avoid distal loop difficulties in cases of imperforate anus, abdominal colostomy is now being carried out with a small bridge of skin separating the completely divided colostomy opening and with the proximal stoma placed caudad to the distal stoma, a policy we have adopted at this institution in all colostomies which we feel are likely to be permanent.

The results in the treatment of Type 4 patients have been most distressing. One of the most pressing problems concerning the management of these cases is the need for earlier recognition. Abdominoperineal operation, theoretically, provides the most rational approach to the treatment of Type 4 anomalies, al-

though we have not as yet had the opportunity to utilize it. Patton[19] has recently reported the successful anastomosis of the anal to the rectal pouch through an abdominal incision in a 14-month-old patient upon whom a sigmoid colostomy had been performed at birth.

SUMMARY

1. The literature pertaining to the surgical management of congenital malformations of the rectum and anus is reviewed.

2. The experience with 120 cases of congenital malformations of the rectum and anus during a 25-year period is reported.

3. The frequency and the sex, racial, and familial incidence of anorectal abnormalities are discussed.

4. The types of malformation are presented according to the accepted classification of Ladd and Gross and the clinical measures utilized in classifying patients are discussed. Five of the patients were of Type 1, 20 of Type 2, 90 of Type 3, and 5 of Type 4.

5. Congenital fistulas between the blind end of the hindgut and the bladder, urethra, perineum, or vagina were found in 70 of the 120 cases (58 per cent).

6. Additional congenital anomalies were encountered in 86 of the 120 patients (72 per cent) and in 33 of the 34 patients upon whom post-mortem studies were carried out (97 per cent). These associated anomalies accounted for close to one-half of the fatalities in this series.

7. The surgical measures employed in the management of the various types of malformation are presented and the results analyzed. Abdominoperineal anoplasty has been carried out without operative mortality in 11 cases of Type 3 malformations. The reasons for abandoning perineal anoplasty in favor of combined abdominoperineal anoplasty in the care of Type 3 patients, those with high rectal pouches, are given.

8. The suspicion, based on studies currently in progress, that distal colonic motility may be congenitally deficient in some patients with anorectal anomalies has led us to adopt a policy of routinely carrying out frozen section microscopic studies for myenteric plexus ganglion cells on the terminal colonic segment during abdominoperineal anoplasty, before using it for pull-through mucocutaneous suture.

9. Complications, particularly colostomy difficulties and the occurrence of intussusception, are discussed.

10. Fifty of the 120 patients (42 per cent) have died during the period covered by this study. All deaths have been included regardless of the cause or the length of time following operation. The factors contributing to the high long-term mortality are given.

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DISCUSSION

DR. ROBERT GROSS.—Anyone who has had extensive experience in this field fully realizes the number of facets to the imperforate anus problem which Dr. Moore and Dr. Lawrence have summarized so well. I commend them on their review.

Over a period of many years, a series of 510 cases have been operated upon by various men on the visiting and house staffs of our hospital. In the last three years, the total mortality rate has been 11 per cent. Analysis of this figure shows that other severe anomalies were responsible for the majority of the deaths. Fatalities primarily related to other anomalies accounted for 7.4 per cent and fatalities due directly to the surgical attack on the anal rectal anomaly itself totaled 3.6 per cent.

Regarding abdominoperineal repairs, toward which Dr. Jonathan Rhoads directed our attention in 1948, certain remarks are in order. We have performed 76 of these; there have been four deaths. An evaluation of the procedure gives us the following facts and impressions. First, it is possible to pull down a rectal pouch, no matter how high it is. Second, it is possible to form in all cases an anal opening devoid of stricture. Third, the fistula problem—which used to be so serious—has now completely disappeared, because fistulas in all these subjects can be permanently closed at the one operation. Fourth, there is variability regarding the attainment of anal continence. Regarding this last point, our general impressions are about as follows: probably 70 per cent of the children have good anal sphincteric action. There are about 15 per cent who have been operated upon so recently that they cannot be evaluated as yet. There are a final 15 per cent who apparently will never have any anal sphincter tone; the anus is patulous, there is incontinence and there is

little hope that much will ever be gained in the way of control. Even so, we do not feel entirely pessimistic about this latter group because, while it might be difficult to handle the situation in the first few years of life, we have found it possible in older children to give a constipating diet, combined with daily rectal lavage, handling the matter in a way which has been so well established for the care of an abdominal colostomy. While the abdominoperineal operation should not be undertaken if the anomaly can be corrected by a simpler perineal procedure alone, it can be carried out, as Dr. Moore has shown, with a very low mortality rate and with over-all results which are generally quite good but which are sometimes a little disappointing as far as continence is concerned.

DR. C. EVERETT KOOP.—I can add just one thing to what Dr. Gross has said. Inasmuch as Jonathan Rhoads began the abdominal perineal pull-throughs in our clinic, we have had just a little more time to practice it and have done now about 60 such procedures. Of these, about 22 or 23 have been done for a longer period of time than three years which means that they should have ordinarily established bowel control and, of these 22 or 23 patients, we have only two with completely patulous perineal colostomies. I would think that with the passage of time this would prove to be a very satisfactory procedure.

DR. EDWIN A. LAWRENCE.—While I was listening two days ago to the beautiful presentation by Dr. Duraiswami on the abnormalities produced by the chicken embryo by hormonal manipulation, I could not help but wonder what, if any, similar intrauterine hormonal manipulation was responsible for these abnormalities that assume such catastrophic proportions. Dr. Moore mentioned briefly an interest of ours in the neurogenic difficulties associated with this problem, as they are applied to the distal colon and also to the urinary apparatus. I should like to present 3 slides on a patient in his series that has interested us and, I might also say, has confused us. The first slide is a reflux urogram of a patient who was demonstrated to have had hydronephrosis and hydro-ureter by intravenous pyelography. The infant came to post mortem and the next slide shows the bladder with the ureteral orifices. On your left is the normal right ureteral orifice and, on your right, is the orifice of the left hydro-ureter. It was just as wide open as it seems to be in this demonstration. There was no constriction, no band, no hypertrophy of musculature at the junction of the ureter and bladder. A section was removed from this area for microscopic study and the next slide shows this large, apparently normal, ganglion in the adventitia, not in the muscle layers, but in the adventitia. Other ganglia were present in the same section.

DR. MOORE (Closing).—I should like to thank Dr. Lawrence, Dr. Gross, and Dr. Koop for their kind and instructive remarks. With respect to the problem of perineal anoplasty, we do carry out this procedure in Type 2 patients, those with relatively low rectal pouches. In all but 1 of the 11 abdominal perineal anoplasties, the pouch was quite high. It is of interest that transabdominal division of an unimportant vascular bundle was necessary in the 1 borderline case to achieve a really adequate mucocutaneous approximation without tension. Concerning the functional success of perineal anoplasty, the ratio of good to poor results will depend, to a degree, upon the criteria employed. The finding that some patients with recurrent fistulas or "perineal colostomies" are able, with the passage of years, to develop increasing control of bowel movements indicates that the criteria should be sufficiently rigid to exclude these cases if the evaluation is to be meaningful. The demonstration of a functional anal sphincter on examination and the ability to retain even liquid stools are essential criteria. Accordingly, the results with perineal anoplasty have been excellent in Type 2 patients whereas they have been generally poor in those of Type 3.

A NEW CONCEPT OF THE PATHOLOGY OF MEGALOURETERS

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IDIOPATHIC megaloureters is a rare disease entity and its etiology is obscure. Because it is not associated with a demonstrable mechanical ureterovesical obstruction, the generally accepted idea has been that the pathology is in the ureters. Treatment in the past has consequently been directed to the ureters, in the form of partial ureteral resection and reimplantation of the ureters into the bladder. This procedure has produced no consistent and lasting improvement. Recent studies of megaloureters in association with Hirschsprung's disease have suggested bladder dysfunction as the source of the ureteral dilatation. Cystometry studies of patients with Hirschsprung's disease have revealed that about 50 per cent have megalobladders, with diminished or no detrusor contractions. Intravesical pressure in some megalobladders has been elevated to twice that recorded in normal bladders, and in these there has been dilatation of the ureters as well. Since Hirschsprung's disease and idiopathic megaloureters are rare, their concurrence suggests a common etiology.

The pathology in Hirschsprung's disease is an absence of Auerbach's plexus in a varying segment of distal colon, and physiologic studies have demonstrated that the aganglionic bowel is devoid of peristalsis.[1] The absence of an organized propulsive force amounts to a functional obstruction, with dilatation and hypertrophy of the proximal colon as the result of this congenital anomaly. The consistent location of the aganglionic lesion in the rectum and rectosigmoid in Hirschsprung's disease indicates that the malformation is in the pelvic parasympathetic system and in some instances might well involve the urinary bladder whose detrusor muscle is innervated by this portion of the autonomic system. Such a hypothesis would offer an explanation of Hirschsprung's disease whether associated with a normal urinary system or with an abnormal one. It seems plausible that in some cases only the portion of the parasympathetic system that supplies the bladder might be involved.

In such patients there would be a normal colon with a megalobladder, and sometimes with megaloureters. This is probably the explanation of some of the cases of so-called "idiopathic" megaloureters. The finding of an abnormality of the parasympathetic system of the bladder would support this hypothesis.

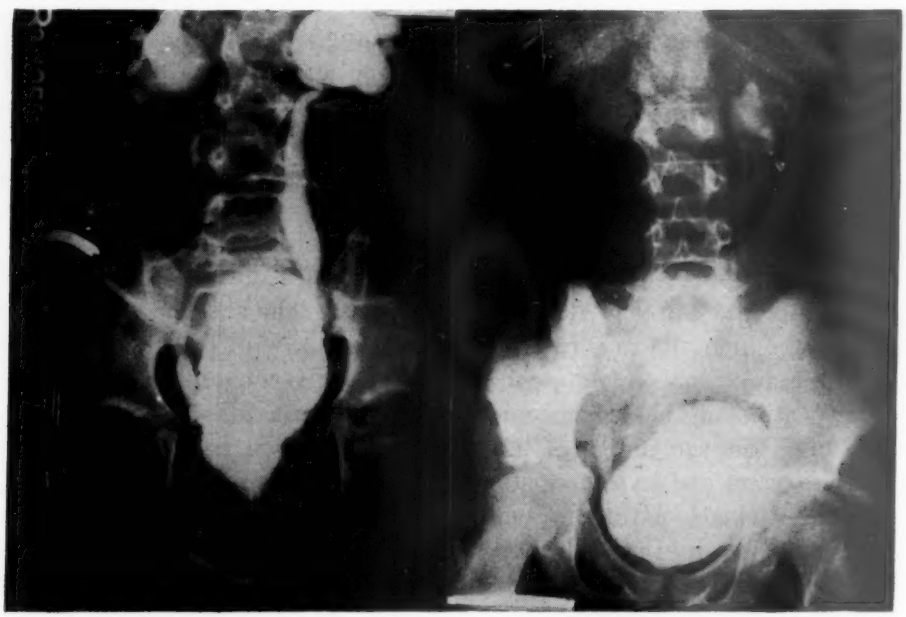
In a study of nine normal bladders, the distribution of ganglion cells was found to be clusters in the periureteral areas, with a rapid diminution toward the midline anteriorly and posteriorly. A similar decrease was seen toward the urethra and fundus of the bladder. Previously, examination had been made of seven bladders from patients with clinical manifestations and characteristic findings, at autopsy, of megaloureters. In six there was a clear-cut diminution of

Read at the meeting of the Society of University Surgeons, Baltimore, Md., Feb. 7-9, 1952.

ganglion cells, which made it possible to segregate them consistently from the normal bladders.[2] In the seventh, the diminution of ganglion cells was not so conclusive. A more recent study of one additional bladder from a patient with Hirschsprung's disease also disclosed a conclusive decrease in ganglion cells.

If the hypothesis that bladder dysfunction is an important factor in the production of megaloureters is true, then bladder drainage should improve the megaloureters.

In four of a series of eight patients, striking improvement occurred by this means (Fig. 1). Of the remaining four patients, one, after initial improvement, had regression due to a stone which intermittently blocked the lower end of the ureter. The kidney on the other side had practically no function. Two patients with elevated blood nonprotein nitrogen had some improvement but the renal function by this test did not return to normal.



A. *B.*

Fig. 1.—*A*, Roentgenogram of a patient with megaloureters before suprapubic drainage. *B*, Repeat film after eight months of suprapubic drainage. (From New England J. Med.)

Nephrostomies on one of the patients with elevated nonprotein nitrogen revealed bilateral, hypoplastic, malformed kidneys. The last patient in this group improved somewhat and then developed severe bladder discomfort and bladder drainage was discontinued.

Further evidence of bladder dysfunction has been demonstrated by careful cystometry studies. Normal bladders have active detrusor contractions as the limit of filling is approached. Between contractions, however, the intravesical pressure returns to a base line usually not exceeding 10 or 12 cm. of water. In Hirschsprung's disease the bladders in some cases have an increased capacity;

there are few, if any, detrusor contractions; and in those instances in which the intravesical pressure rises from 20 to 30 cm. of water, there have been megaloureters (Fig. 2).

In two patients, active peristalsis was present in the megaloureters and the pressure was normal. Three other patients with megaloureters were observed to have active peristalsis, but no pressure recordings were obtained.

DISCUSSION

From a physiologic standpoint there are four defects that could be present in a bladder with impaired parasympathetic innervation.

First, and probably of most importance, is failure of the detrusor to relax as filling occurs, which would be an obstacle to the injection of urine from the ureter into the bladder. Over a long period of time, the alteration in dynamics caused by intravesical pressure twice the normal would probably affect ureteral function and play a large role in ureteral dilatation.

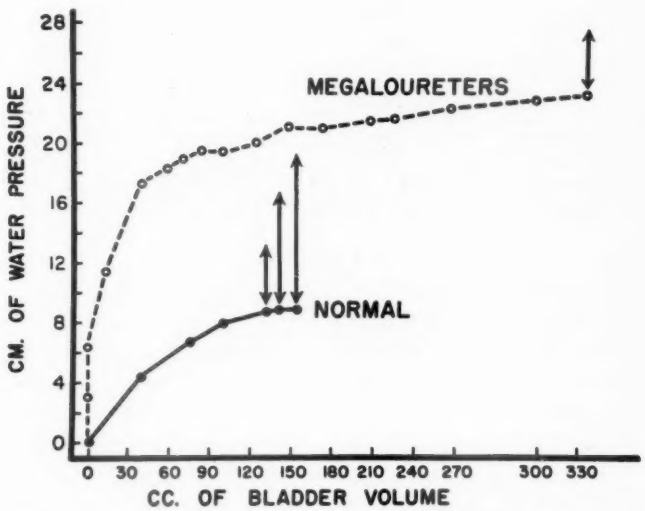


Fig. 2.—Cystometrograms on a patient with megaloureters and on a normal subject. Note that the intravesical pressure in the patient with megaloureters is twice as high as that in the normal patient.

Second, improper relaxation of the bladder outlet during micturition would make voiding difficult and promote a residue of urine.

Third, faulty detrusor contractions would result in poor emptying.

Fourth, failure of the ureterovesical junction to relax as the ureteral peristalsis approached the bladder would be a direct burden on ureteral function.

We believe all of these defects play a role in the formation of megaloureters. A complete investigation of a patient with megaloureters should include a cystometrogram, urethrogram, cystogram, intravenous urogram, and a determination of residual urine. Urethroscopic examination to rule out mechanical obstruction, and cystoscopy for demonstration of free ureterovesical junctions and determination of ureteral peristalsis and pressure should be performed.

Treatment should be directed toward establishment of better bladder function. Megalobladders are overdistended but much return of function can be secured by suprapubic drainage over a period of from four to six months. The bladders then have a smaller capacity, and if the child is cooperative he can be taught to void five or six times a day and use suprapubic pressure in an effort to completely empty the bladder. We have had good return of function in such cases, particularly if the nonprotein nitrogen is not elevated. How well this disease can be controlled by these methods can only be determined after a longer period of observation.

SUMMARY

Megaloureters are occasionally associated with Hirschsprung's disease. This suggests a common congenital anomaly in the pelvic parasympathetic system. A diminution in ganglion cells of the bladder has been found in patients with megaloureters.

There has been improvement with bladder drainage.

This evidence suggests that a group of patients with idiopathic megaloureters have bladder dysfunction as the basis of their disease.

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DISCUSSION

DR. HARRIS B. SHUMACKER, JR.—Dr. Swenson has presented a most interesting and valuable piece of work. I think that it will be important to study very carefully along the basis he has suggested not only cases of megaloureter but the not infrequent examples of distended bladder with residual urine and without megaloureter as well. It will be interesting to follow these cases and to learn whether, if untreated, they will subsequently develop megaloureter and, if so, whether such changes can be avoided by proper early treatment.

DR. KEITH S. GRIMSON.—I would like to congratulate the author on an excellent study and a good idea. In principle, of course, our observations with regard to etiology of achalasia and megacolon differ from Dr. Swenson's only in a detail: Is the myenteric plexus absent or is it only damaged or functioning abnormally? Although we have no experience with megaloureter there is a common interest when any lesion of the parasympathetic nervous system is considered. The postganglionic plexus of the parasympathetic nervous system to most viscera, like the myenteric plexus in the intestine, is usually composed of a postganglionic group of cells with short fibers located within the visceral wall. The preganglionic fibers are long. Histologically, it may be extremely difficult to demonstrate and identify the ganglia of the myenteric plexus. Therefore failure to demonstrate ganglia or demonstration of absence of ganglia by histologic methods is, at best, indirect evidence.

It is acknowledged that the demonstrations presented are good and that the histologic techniques are probably accurate. There is, however, another method of obtaining evidence: use of manometric techniques—balloons or cystometrograms—and of parasympathomimetic drugs. Preganglionic denervation usually leads to an increase of resting tone of a hollow viscus, which I believe was demonstrated. Theoretically, absence of ganglia would lead to loss of tone, perhaps dilatation. In the intestinal tract, peristalsis continues in the absence of preganglionic innervation because of activity of the myenteric plexus. It would stop if

there were absence of ganglia. Specialized functions such as the valvular and ejection actions at the pylorus, the rectum, and the lower end of the esophagus are partially dependent upon preganglionic innervation. According to these principals manometric techniques might be used to confirm the studies by Dr. Swenson and determine whether the lesion is pre- or postganglionic and loss of function complete or partial. Also use of parasympathomimetic drugs would be helpful for, if ganglia cells are absent, administration of Urecholine should not produce a response. If ganglia cells are present, then administration of Urecholine should stimulate propulsive activity of the hollow viscus. If the ganglia cells are present although damaged or functioning abnormally and Urecholine produces peristalsis, then this drug could be used as a method of therapy to supplement other measures. Our experience has been that doses of 15 to 30 mg. orally do aid many patients with megacolon and that surgery for this condition is seldom necessary.

DR. SWENSON (Closing).—We are very much interested in the use of drugs in the study of megaloureters, and we have started some experiments to determine their possible value. However, we have no data for presentation at this time. I want to thank the two discussers.

FUNCTIONAL RESULTS OF SMALL INTESTINAL SEGMENTS AS BLADDER SUBSTITUTES FOLLOWING PELVIC EVISCERATION

A Progress Report

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THE continued investigation of pelvic evisceration for postirradiation recurrent carcinoma of the cervix has afforded an opportunity to evaluate the methods of bladder substitution which are a necessary part of this procedure. Since April, 1950,[1] we have elected to transplant the ureters into short isolated segments of terminal ileum which in turn are emptied through the abdominal wall of the right lower quadrant in an area convenient for the application of a Rutzen bag. The urinary stream is thus isolated from the fecal stream and traverses the intestinal tract through only a short segment of small intestine which acts merely as a conduit and not as a reservoir. We have found this method of handling the ureters to be very satisfactory. Those patients who have the bladder substitution associated with pelvic evisceration have a colostomy opening on the left side of the abdomen. From the aesthetic standpoint, this arrangement has permitted the patients to keep themselves clean and odorless with a minimum of difficulty. The care of the Rutzen bag and the disposal of urine from it is a simple procedure. Mersheimer and associates[11, 12] have approached this problem independently in experimental animals for essentially the same reasons that have prompted our own efforts.

PURPOSE AND MATERIAL

Previous reports have dwelt upon the development of this method of bladder substitution and upon the infrequency of early postoperative complications.[1-4] An evaluation of methods of bladder substitution has become more important since it appears that pelvic evisceration may evolve into a therapeutic procedure of some value, and since the recent discovery that ureterosigmoidal anastomosis following cystectomy alone results in a high incidence of complications in the form of hyperchloremia and acidosis.[7, 8] It is the primary purpose of this paper to present, as a progress report, the results of fifty-five bladder substitution procedures (Table I). Twenty-eight of these patients have gone for periods of six to twenty-two months since operation and have had recent pyelographic studies. These twenty-eight patients form the basis of the study of late functional results. Fourteen of the fifty-five patients have been contributed by Dr. John Modlin of The Ellis Fischel State Cancer Hospital in Columbia, Missouri.

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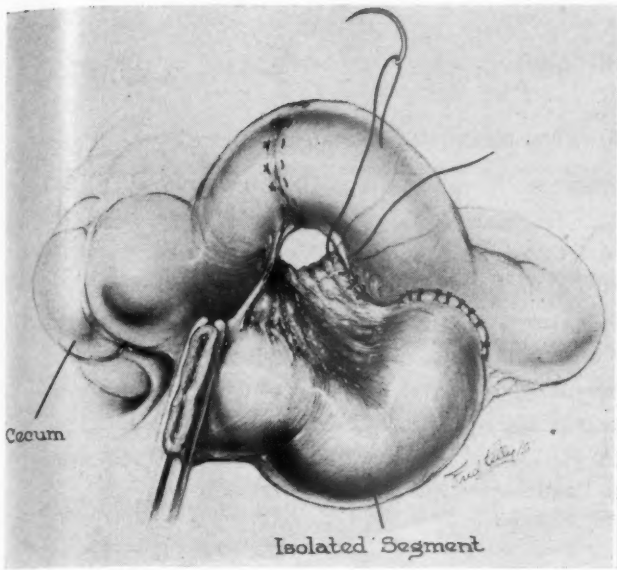


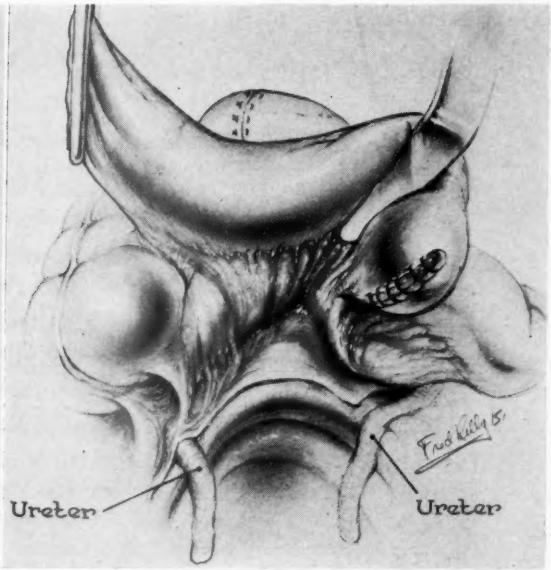
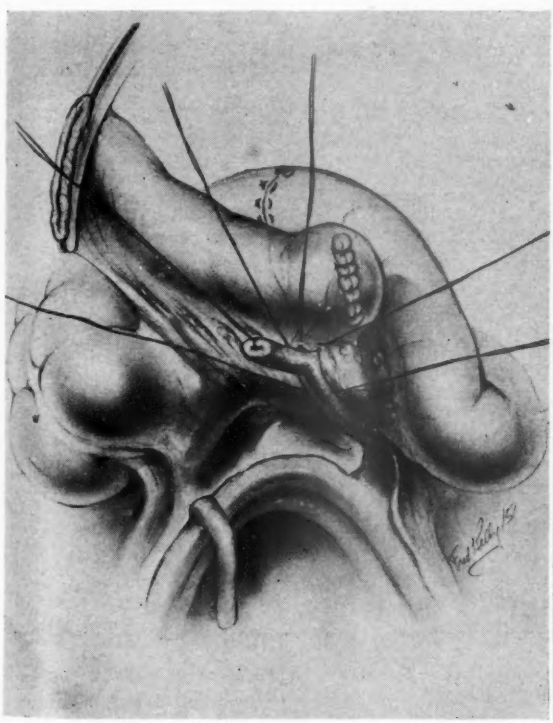


Fig. 1.—The intestinal segment is isolated from the terminal ileum about 4 to 6 in. from the ileocecal junction. A segment of 6 to 8 in. in length is necessary to reach from the promontory of the sacrum to the skin of the right lower quadrant in a position that will comfortably hold a Rutzen bag. The appendix is always removed if present. The rent in the mesentery of the small intestine is carefully repaired. The continuity of the ileum is re-established by end-to-end anastomosis with two rows of interrupted fine cotton or silk.

Fig. 2.—The relationships of the ureters to the isolated segment are ideal for simple mechanical approximation. The ureters are usually sectioned 2 or 3 cm. below the level of the iliac arteries.



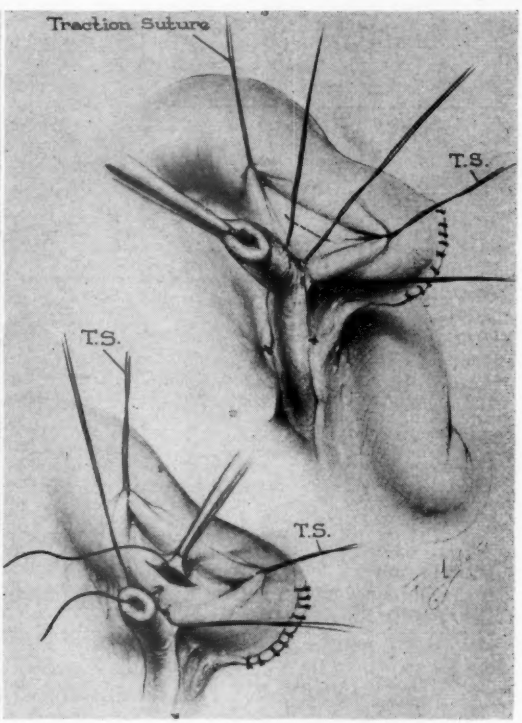


Fig. 3.—The left ureter is very carefully sutured to the under surface of the mesentery of the isolated segment in such a manner as to obliterate the tunnel through which the small intestine could easily herniate. This precaution is not always taken with the right ureter which is in a more protected position beneath the mesentery of the small intestine. The fixing sutures are placed in the adventitia of the ureter and the ureter is finally fixed to the mesenteric border of the small intestine by a row of three or four sutures which form the outer layer of the anastomosis.

Fig. 4.—The anastomosis is completed after a small opening is made through the serosa and into the mucosa of the small intestine. Interrupted sutures are used through the ureter and through the mucosa of the bowel. For suture material the finest silk or catgut is used for this inner row. Six to eight sutures are usually placed around the circumference of a normal-sized ureter. The external layer, or the adventitial sutures, is then completed around the circumference of the anastomosis. Care is taken not to include too much ureter in any of the sutures or to excessively invaginate the ureter into the bowel.

TABLE I. BLADDER SUBSTITUTION WITH SMALL INTESTINAL SEGMENTS

Total bladder substitution procedures		55
With pelvic evisceration	46	
With cystectomy	4	
Palliative (bladder substitution alone)	5	
Not included in study of late complications		27
Died of operation	9	
Less than six months' follow-up	11	
Expired of recurrent cancer before six months	1	
Lost to follow-up (palliative)	2	
Six months' pyelograms not available	4	
Followed for six months or longer		28

TABLE II. CLASSIFICATION FOR RESULTS OF BLADDER SUBSTITUTION
(Six Months' Minimum Follow-up)

Classification by individual renal units (intravenous pyelograms)
Normal—Normal intravenous pyelogram
Grade I—Minimal hydronephrosis
Grade II—Definite hydronephrosis
Grade III—Massive hydronephrosis
Grade IV—Nonfunctioning kidney by intravenous pyelograms

Classification by Individual Patient (intravenous pyelograms plus clinical evidence of pyelonephritis)
Satisfactory—Those patients never having had clinical evidence of pyelonephritis and with pyelograms showing no worse than Grade I hydronephrosis on either side
Unsatisfactory—All patients having at any time in their clinical course shown definite evidence of pyelonephritis or with pyelograms showing hydronephrosis of Grade II or worse on either side

TABLE III. INDIVIDUAL RENAL UNITS (FIFTY-FIVE)

	ALL URETERS (55)		NORMAL URETERS (35)		HYDRONEPHROTIC URETERS (20)	
	PREOP.	POSTOP.	PREOP.	POSTOP.	PREOP.	POSTOP.
Normal	35	26	35	18		8
Grade I	5	13		7	5	6
Grade II	4	5		3	4	2
Grade III	4	8		7	4	1
Grade IV	7	3			7	3

TABLE IV. INDIVIDUAL PATIENTS (TWENTY-EIGHT)

Satisfactory		
Normal or Grade I renal units and no pyelonephritis		17
Bilateral normal renal units	9	
Unsatisfactory		
Pyelonephritis or Grade II renal units or worse		11
Pyelonephritis	8	

TABLE V. PYELONEPHRITIS (EIGHT PATIENTS OF TWENTY-EIGHT)

Bilateral normal renal units		0
Normal or Grade I renal units		2
Grade II or worse renal units		6
Time of onset of symptoms of pyelonephritis		
1. 7 months	5. 11 months	
2. 4 months	6. 3 months	
3. 2 months	7. 5 months	
4. 12 months	8. 15 months	

TECHNICAL PROCEDURE

The technique of the bladder substitution procedure has changed little since it was first developed.[1] The essential technical points are outlined in the legends of the accompanying illustrations (Figs. 1 to 5). We no longer deem it necessary to obliterate the right lumbar gutter by suturing the isolated segment of small intestine to the parietal peritoneum as was first described. On the other hand, we feel it important to suture the ureters to the under surface of the mesentery of the small bowel to prevent internal herniation (Fig. 3). The operating time required to isolate an intestinal segment, to do an end-to-end anastomosis of the bowel, and to anastomose both ureters to the intestinal segment

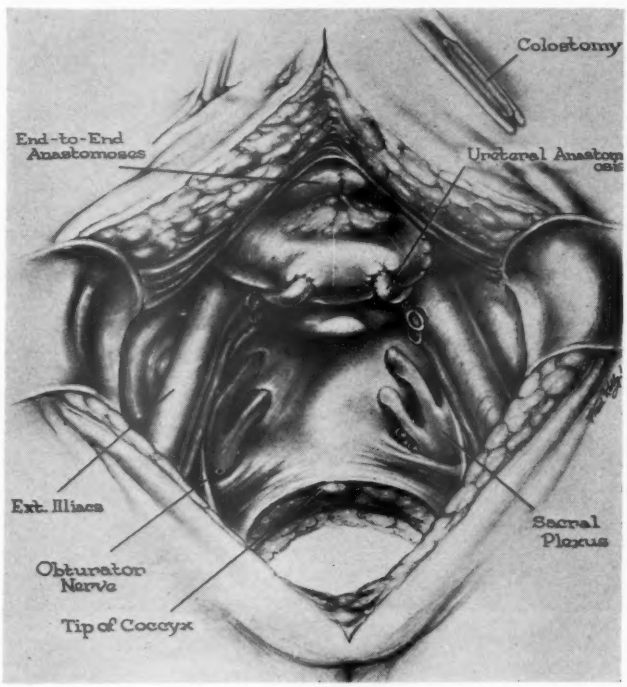


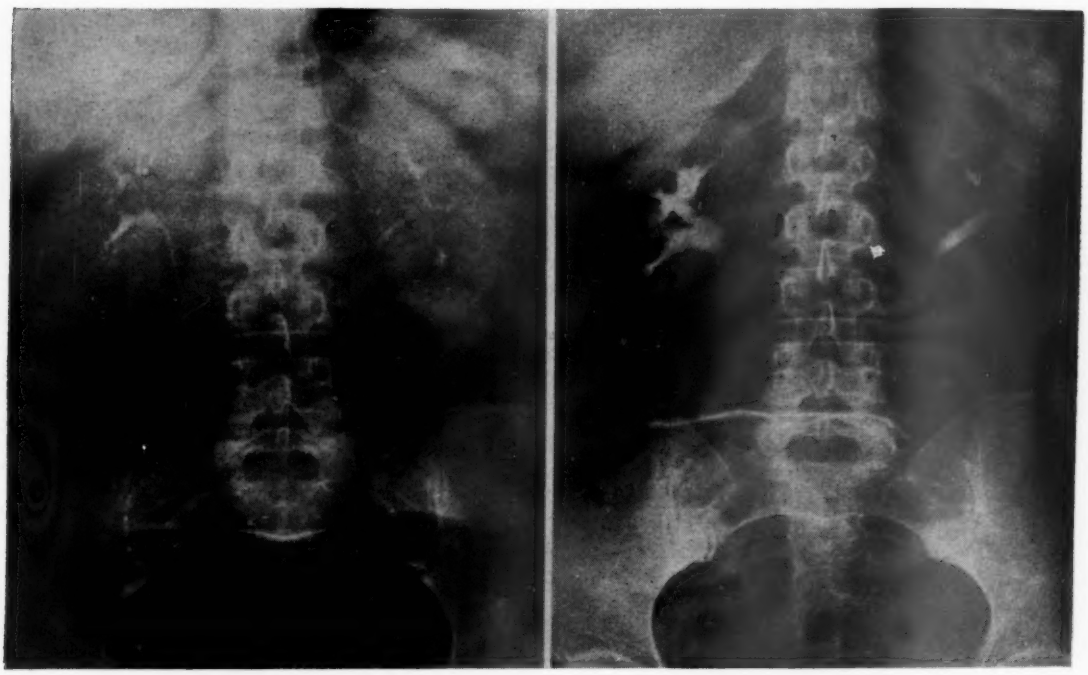
Fig. 5.—After completion of the anastomoses the ileal segment should rest naturally in an advantageous position to receive the ureters without kinking or distortion. This illustration shows the usual position of the isolated segment with the ureters anastomosed to it at the level of the sacral promontory. The external stoma of the segment is opened immediately and very carefully sutured to the skin edge of the accessory incision. It is important that an adequate incision through the abdominal wall be made in order that no obstruction of the ileal segment will occur at this level.

has been only sixty to seventy-five minutes. The entire substitution procedure can be done at wound level without additional abdominal dissection or retraction. These latter points are of obvious importance if the procedure is being associated with extensive pelvic surgery.

FOLLOW-UP STUDY

Mortality.—Of the nine operative deaths in this series of fifty-five patients having had bladder substitution (Table I), only two have been directly attributable to the bladder substitution procedure per se. One of these resulted in death on the twenty-eighth postoperative day from acute pyelonephritis. This patient

had presented bilateral hydronephrosis and pyelonephritis preceding operation. The second death occurred as the result of a breakdown of the end-to-end anastomosis of the small intestine. Two patients expired after having had severe convulsive seizures from an unexplained cause. It is of interest that each of these patients had only one functioning kidney at the time of operation and the cause of convulsions was not disclosed by the subsequent clinical course or by post-mortem examination. Convulsions were also a notable feature in two other patients, one of whom recovered completely, the other being the patient



A. *B.*

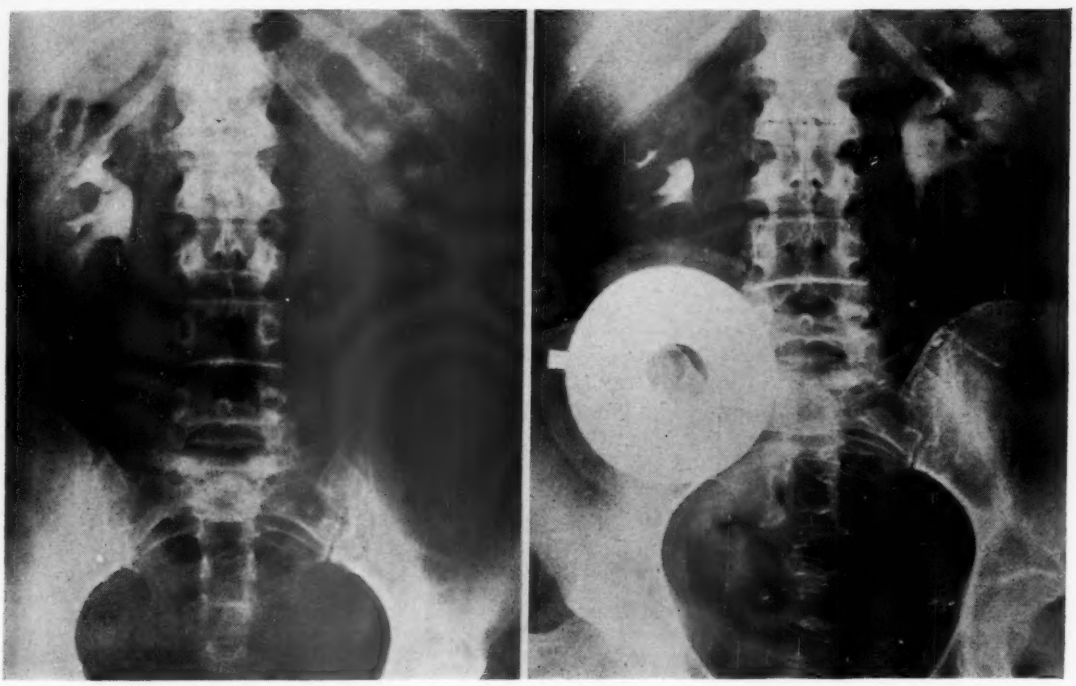
Fig. 6 (Patient L. M.).—*A*, Preoperative pyelograms bilaterally normal. *B*, Pyelograms eight months following operation classified as normal. The radiopaque material appeared promptly and the calices are sharply defined and not dilated. The ureters empty promptly. This patient has not had an episode of infection and is classified as having a satisfactory result. A similar result was obtained in seven of twelve patients having preoperatively normal pyelograms.

who expired of acute pyelonephritis. It is impossible to state accurately the mortality of bladder substitution in this series since in all but five instances the procedure was only an incidental part of more extensive surgery.

Early Nonfatal Postoperative Complications.—Forty-six patients have survived the procedure of bladder substitution and the related resection. An earlier report has presented the nonfatal complications occurring in twenty-five of these patients.[2] Three patients have had postoperative intestinal obstruction relieved in each instance by conservative nonoperative measures. There has been no instance of urinary fistula. Early postoperative azotemia has never been a problem. A transient anuria appearing forty-eight hours after operation in one patient was interpreted as being due to temporary obstruction of the

anastomoses from edema. Severe early postoperative hydronephrosis has occurred only once. In this patient the condition was bilateral and necessitated reoperation after four months.

Late Complications (Six to Twenty-two Months).—In evaluation of late results, attention has been directed chiefly at detecting evidence of ascending urinary tract infection, at an evaluation of the technical result as determined by repeated intravenous pyelograms, and in searching for evidence of electrolyte imbalance. The occurrence of a single episode of chills and fever associated with flank pain and tenderness at any time in the postoperative course has classified the patient as having pyelonephritis and the patient remains so classified regardless of the clinical course subsequent to the initial infection. This rule



A. *B.*

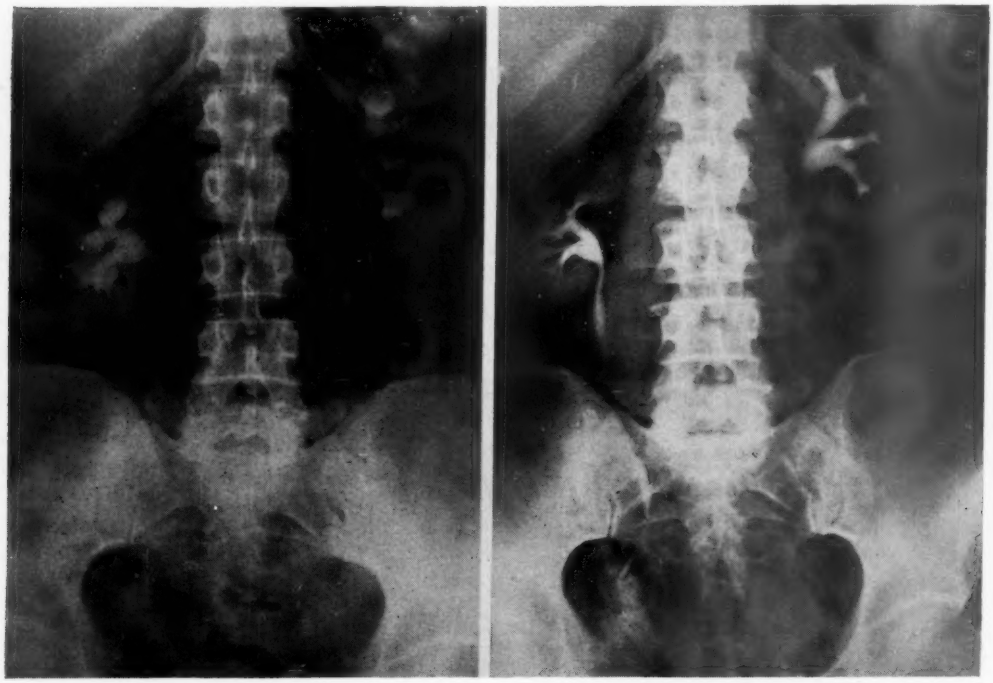
Fig. 7 (Patient J. S.).—*A*, Preoperative pyelograms showing normal right kidney and a Grade III hydronephrosis on the left.

B, The pyelograms six months after operation, normal on the right and Grade I, or minimal, hydronephrosis on the left. No episode of infection. Classified as satisfactory result.

is adhered to strictly since the study should provide for perfectly clear recognition of the patients who do *not* develop infection subsequent to the procedure. Similarly, the evaluation of pyelographic studies should clearly indicate the perfect and nearly perfect results. This can be accomplished most satisfactorily by adopting the plan used by Marshall[9, 10] of reporting the results by individual renal units, rather than by patients, or pairs of renal units (Table II). Finally, a combination of the roentgenologic findings with the clinical picture of infection or absence of infection has seemed to be the only means by which the truly satisfactory clinical results can be selected. Table II is self-explanatory and has

formed the basis for the study of our twenty-eight patients. Figs. 6 to 10 give illustrative examples of the various grades used in the classification of renal units and of individual patients.

Hydronephrosis.—The results of individual renal unit studies of postoperative pyelograms and a comparison with the preoperative status of these twenty-eight patients are submitted in Table III.* One renal unit complicated by the development of carcinoma of the kidney pelvis after the palliative resection of a massive bladder carcinoma is omitted from this study. It is of interest that of all fifty-five ureters transplanted, thirty-nine fell within the limits of normal



A. *B.*

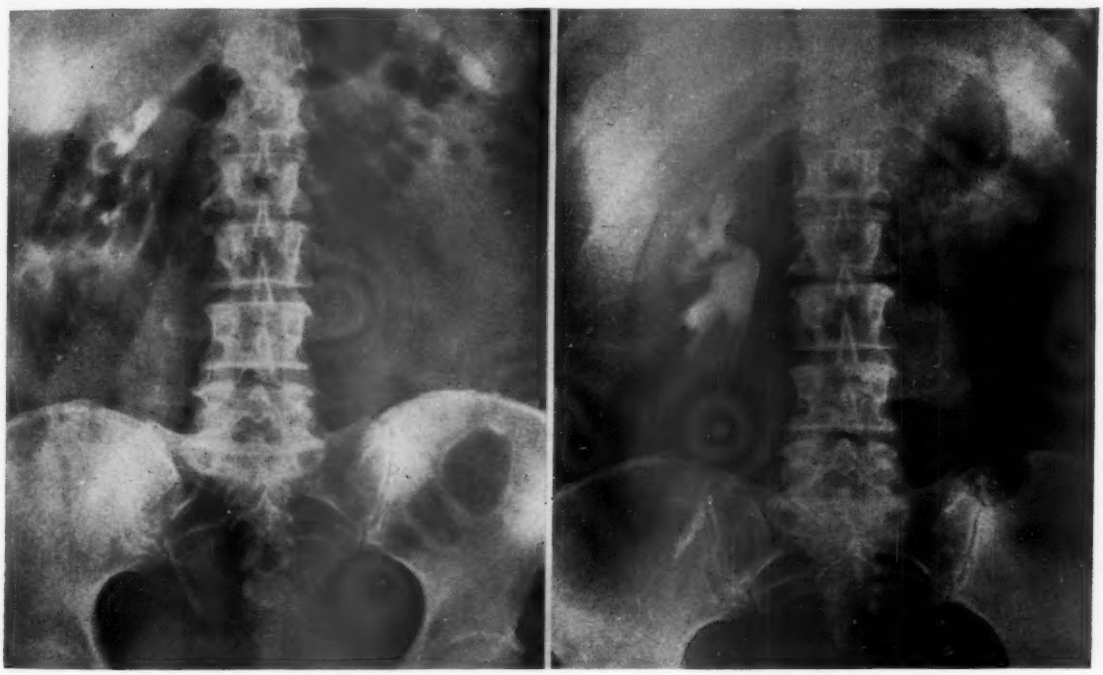
Fig. 8 (Patient G. P.).—*A*, Preoperative bilateral hydronephrosis of Grade III severity. *B*, Six months postoperative pyelograms showing Grade I hydronephrosis on the right and Grade II on the left. This patient has never had an episode of infection but she is listed as having an unsatisfactory result since a Grade II hydronephrosis still exists in the left kidney.

or Grade I hydronephrosis. Of thirty-five preoperatively normal ureters, twenty-five fell into the normal or Grade I category and seven showed a marked hydronephrosis. Transplantation of hydronephrotic ureters resulted in a marked upgrading with the exception of three renal units that remained nonfunctional at six months. Although the number of transplants is as yet too small to be reliably significant, it is of interest to note that roughly 70 per cent of the transplants have been good (normal or Grade I) whether the calculation is made on all transplants or on the normal and hydronephrotic transplants

*The pyelograms in this study were read and classified by Dr. Justin Cordonnier and Dr. Oscar Zink of the Urology and Radiology Departments, respectively.

separately. There is likewise a 30 per cent chance that a transplant will be poor (Grade II hydronephrosis or worse), and each patient with two kidneys takes this risk twice. It is promising for the procedure that these figures compare so favorably with Marshall's[10] figure of 46.9 per cent good results in a comparable classification of seventy-nine ureteral transplants.

Pyelonephritis.—In considering the results of bilateral ureteral transplantation in individual patients (Table IV) the occurrence of ascending infection is taken into consideration. Twenty of the twenty-eight patients have been without clinical evidence of infection for six months or longer. However, three of these patients have hydronephrosis of Grade II severity or worse, involving one or both kidneys, and are therefore relegated to the "unsatisfactory" group.



A. *B.*

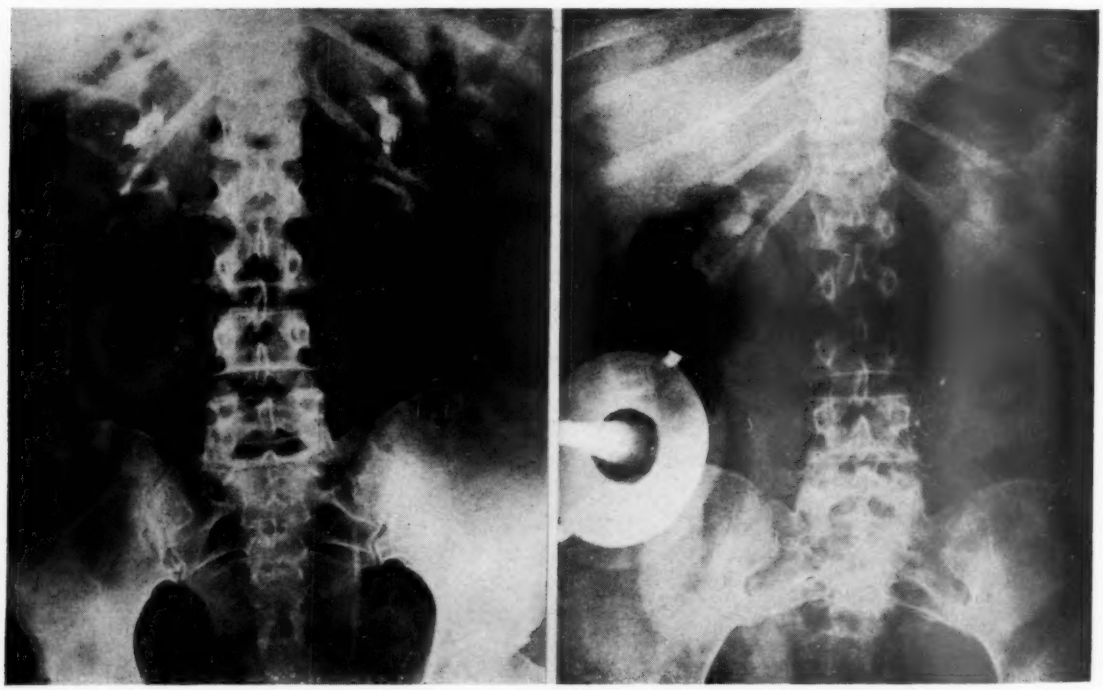
Fig. 9 (Patient J. D.).—*A,* Preoperative pyleograms show nonfunction on the left and a normal right kidney.

B, Six months later there is still nonfunction on the left and the right kidney shows a Grade I hydronephrosis. There has been no clinical evidence of pyelonephritis. In this series there have been seven kidneys nonfunctional by preoperative pyelography; four have shown a return of function. If there is no infection the patient with a persistently nonfunctional kidney is classified as satisfactory if the opposite kidney is normal or only Grade I. Two such patients, including the one illustrated here, are classified as satisfactory.

The chance of subsequent development of pyelonephritis in these patients is considered to be very great. No patient with bilateral normal pyelograms has yet had clinical evidence of infection (Table V). Of the eleven patients placed in the unsatisfactory category, two had renal units that were normal or Grade I and would have been included in the satisfactory group had it not been for the occurrence of an episode of infection. Six of the eight patients developing pyelonephritis had renal units of Grade II or worse.

Cultures of urine from the ileal segments have revealed chiefly organisms of the coliform group. From two patients with clinical evidence of pyelonephritis, pure cultures of *Proteus vulgaris* were obtained. *Pseudomonas pyocyanea* was obtained in pure culture from another patient with no clinical evidence of infection. *Proteus vulgaris* was cultured from the kidney pelves of the patient who died on the twenty-eighth postoperative day as the result of pyelonephritis.

Hyperchloremia and Acidosis.—Blood chemistry studies have been limited to plasma levels of nonprotein nitrogen, bicarbonate, and chloride. The nonprotein nitrogen and plasma bicarbonate levels have been uniformly normal



A. *B.*

Fig. 10 (Patient J. B.).—*A*, Preoperative normal pyelograms bilaterally.

B, One-year postoperative pyelograms showing Grade III hydronephrosis on each side. This patient has had one mild episode of ascending infection easily controlled by antibiotics. Although clinically well twenty-two months after operation, the bladder substitution procedure has been classified as unsatisfactory because of one episode of infection and because of bilateral hydronephrosis of severe degree. This patient had very far-advanced recurrent carcinoma of the cervix when operated upon and is considered as an extremely poor candidate for long-term survival. If it were not for this fact, reoperation for relief of the bilateral hydronephrosis would be seriously considered.

except in the one patient with early bilateral ureteral obstruction requiring reoperation. The picture of infection was predominate in this patient, but blood chemistry studies revealed an elevation of plasma nonprotein nitrogen and chloride with a depression of plasma bicarbonate suggestive of "hyperchloremic acidosis." Several patients have shown a mild elevation of plasma chloride but in no instance except the one cited above was this elevation associated with a lowering of the bicarbonate level.

DISCUSSION

The low incidence of early complications is thought to be attributable to two factors: (1) freedom from continued fecal contamination, and (2) prompt and free evacuation of the urine through the open ileostomy stoma. These same factors may prove to be effective also in reducing the incidence of the late complications of hydronephrosis and pyelonephritis. Klinge[7] has shown that the isolated ileal segments empty by periodic peristalsis initiated by hydrostatic pressure within the segment. With a free opening through the abdominal wall it can be expected that emptying of the segments will be unimpeded and there should be a minimal rise in intraluminal pressure. From the observations of Klinge and from observing the segments directly by fluoroscopy after filling them with barium it is evident that properly constructed ileal segments do not function as intra-abdominal pouches or reservoirs but that they respond promptly to the accumulation of urine within their lumen by the initiation of emptying peristalsis. Stagnation of urine and the development of conditions favorable for unhampered bacterial growth are thus prevented.

The present series is too small to determine whether these factors will materially affect the incidence of pyelonephritis. The relationship between hydronephrosis and pyelonephritis is evident in the patients reported, adding emphasis to the importance of the technical aspects of ureterointestinal anastomosis. It is quite certain that a reduction in ascending infection can best be accomplished by reducing the incidence of hydronephrosis through perfection of the anastomoses. If the incidence of hydronephrosis can be materially decreased it is possible that the frequency of infection may be further reduced through the other theoretically favorable aspects of the isolated small bowel segments. The results of ureteral transplants here reported compare favorably with other series, but there is still an approximately 30 per cent chance that an individual transplant will result in a Grade II hydronephrosis or worse. This chance should be reduced, either by greater perfection of the present technique or by the development of some better method of ureterointestinal anastomosis. It has been our opinion that the present technique of end-to-side, mucosa-to-mucosa anastomosis of the ureter to the clean bowel segment would provide the best conditions for primary healing without obstruction. The results thus far are promising, but not entirely satisfactory or conclusive. More procedures and a longer period of time will be required before the answer can be known.

Eiseman[5] has demonstrated that injected urea and chloride are absorbed from the intestinal segments used as bladder substitutes. It has been our feeling that the amount of intestinal mucosa in contact with urine was so small, and the emptying of the segments so prompt that absorption of urinary constituents would not be a factor of clinical importance. In view of the mild elevation of plasma chloride observed in some of the recent blood chemistries further studies will have to be made before our initial assumption can be verified. If Lapides[8] is correct in believing that hyperchloremia and acidosis are a result of impaired renal function plus the factor of absorption of urinary constituents

through the intestinal mucosa, it is possible that electrolyte imbalance may eventually become apparent in patients with small bowel segments as bladder substitutes.

Rapid, progressive, postoperative hydronephrosis has occurred only once. In this instance the ureters were reanastomosed to the revised ileal segment. The result in this patient has been satisfactory, although the reanastomosis was a difficult procedure. Cutaneous ureterostomy would probably have been easier. It appears that the best solution to the problem of postoperative hydronephrosis is the future improvement of the technique of ureterointestinal anastomosis so that the occurrence of this complication becomes negligible. It is hoped that this can be accomplished.

SUMMARY

The functional results of bladder substitution with small intestinal segments have been presented. Forty-six of fifty-five patients surviving bladder substitution and associated resections have shown a minimum of early nonfatal postoperative complications referable to the procedure. Two of the nine deaths in the series have been directly attributable to complications resulting from the ureteral transplants and small intestinal anastomosis. Convulsions in four patients, three of whom died, have been unexplained clinically or by post-mortem findings.

Of twenty-eight patients with bladder substitutes of six to twenty-two months' duration, seventeen are considered as satisfactory, since they have shown no evidence of infection and the pyelograms reveal normal or only Grade I hydronephrosis on either side. Eight of the twenty-eight patients have developed clinical evidence of pyelonephritis. Of fifty-five ureteral transplants, thirty-nine renal units (70 per cent) have been found to be normal or with minimal hydronephrosis by intravenous pyelography six months or more after operation.

Suggestive laboratory evidence of hyperchloremic acidosis was observed in only one patient who developed bilateral hydronephrosis of severe degree and required reoperation. No other patient has yet been found with a depressed plasma bicarbonate value, though several have had a suggestive elevation of plasma chloride. All plasma nonprotein nitrogen levels have thus far been within the limits of normal except in the case of the patient developing bilateral obstruction.

The experience thus far gained with this method of substitution for the urinary bladder indicates that it has merit, particularly for those patients in whom the rectum cannot be used for this purpose. Continued use of the procedure is justified until the long-term results can be accurately evaluated.

ADDENDUM

Since preparation of this manuscript, a recent patient has developed a perineal urinary fistula from breakdown of both ureterointestinal anastomoses. This patient had previously been subjected to bilateral ureterostomies for relief of complete urinary obstruction. The subsequent ureterointestinal anastomosis was greatly complicated by the previous operation.

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DISCUSSION

DR. MARK M. RAVITCH.—Your Chairman would like to show slides of a child who had not only exstrophy of the bladder but an imperforate anus which had been attacked from below with disastrous results, so that he had a scarred perineal fistula. It was perfectly obvious that, while with what amounted to a perineal colostomy he might achieve a satisfactory result, with training of the type Dr. Gross described the ureterosigmoidal implant treatment of this exstrophy was quite impossible. With Dr. W. W. Scott, Professor and Chairman of the Department of Urology, we prepared an isolated sigmoidal loop within the abdomen. The trigone was divided and each ureteral orifice implanted by an end-to-side anastomosis into the sigmoidal sac which has this phalliform appearance (slide) as the result of the application of a skin graft to the external half of the sigmoid explant in the manner described by Dragstedt for ileostomy, the Rutzen bag seeming not to be quite as convenient a device for a small boy as this plastic urinal. He wears this device very happily. He is going to school and has gone for a year and a half now. You see on your left (slide) the sac filled with the radiopaque medium. In the center, a preoperative roentgenogram showing a quite marked hydronephrosis on the left side—a not uncommon finding in exstrophy of the bladder—and, finally, on the right, what I guess Dr. Bricker would call a Grade I hydronephrosis.

DR. BRICKER (Closing).—A question was just asked me by Dr. Ridgeway Trimble regarding the external stoma of the isolated segment. The distal end of the segment is simply brought out through an accessory incision which is made very loose to insure that no obstruction results. The stoma is then opened and the mucosa is sutured to the skin edge in order to obtain primary healing with a minimum of encircling scar tissue. I would like to point out that our study of the problem of bladder substitution goes back for over ten years and we have consistently failed to develop a really satisfactory intra-abdominal urinary pouch that is continent. For this reason we have dropped all attempts at providing continence and now aim only at conveying the urine as simply as possible to an extra-abdominal receptacle.

STUDIES ON THE REGENERATION OF GASTRIC MUCOSA IN THE EXPERIMENTAL ANIMAL

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ALTERATION of gastric mucous membrane by specific injury, a concept recently enunciated by Howes[1] while investigating the role of mucous cells in the production of gastric neoplasms, has suggested the possibility of a new approach to the study of gastric physiology. Howes observed a differential response of the various cytologic components of the combined gastric mucosa, with respect to their capacity to withstand injury, when the gastric epithelium was injured specifically by ischemia in the presence of hydrochloric acid. Pepsin-producing serous cells and acid-producing parietal cells were noted to be more susceptible to this injury than the basophilic mucous cells. Thus intestinalized mucous-secreting epithelium was produced by regeneration.

Mucous transformation of gastric epithelial cells has been noted previously. In 1901, Cade[2] reported that, after gastroenterostomy in the dog, the glandular elements of the fundic mucosa adjacent to the stoma were altered in such a manner as to suggest pyloric mucosa. In 1906, Harvey[3] confirmed this observation by histologic studies and noted that the serous or pepsin cells in the glands over an area 7 mm. around the new stoma were transformed into mucous-forming cells. He suggested that this phenomenon is a nonspecific reaction to irritation or inflammation and may be seen in connection with ulcer, gastritis, or carcinoma. He felt that it represented a retrogression of cells through their developmental pattern to a more basic cell type. It has been stated that all of the specialized epithelial cells of the gastric mucosa arise from a mitotic focus of basic cells at the bottom of each crypt. Pepsin-forming serous cells and acid-forming parietal cells differentiate as required from the more fundamental mucous chief cells.[4]

It is of interest that although one month after operation Howes' animals had a relative gastric hypochlorhydria, one year after the injury they were secreting gastric juice of pH 1.5 to 2.5 in response to histamine. Harvey also observed that a reversal of the process of mucous transformation around a gastroenterostomy stoma took place within one month after the original operation and that the initial histologic structure of the glands was re-established after six and one-half months.[3] This observation would suggest that mucous transformation is a phenomenon of limited nature and that a slow but per-

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sistent regeneration of the more specialized cells in the gastric mucosa occurs after injury. Howes explained that the return of gastric free acidity in his animals was due to his failure to obtain complete alteration of the mucous membrane by his technique of injuring the mucosa.[1] He stated that after one year there were still extensive areas of intestinalized epithelium but that the residual areas of unaltered mucosa had hypertrophied.

It is interesting to speculate whether the gastric mucosa could be so altered in this manner that it would become entirely and permanently mucus producing. As one phase of his investigation, Howes attempted without success to study the effects of total mechanical destruction of the mucosa of the rat. His failure was apparently due to the high mortality rate which resulted from the

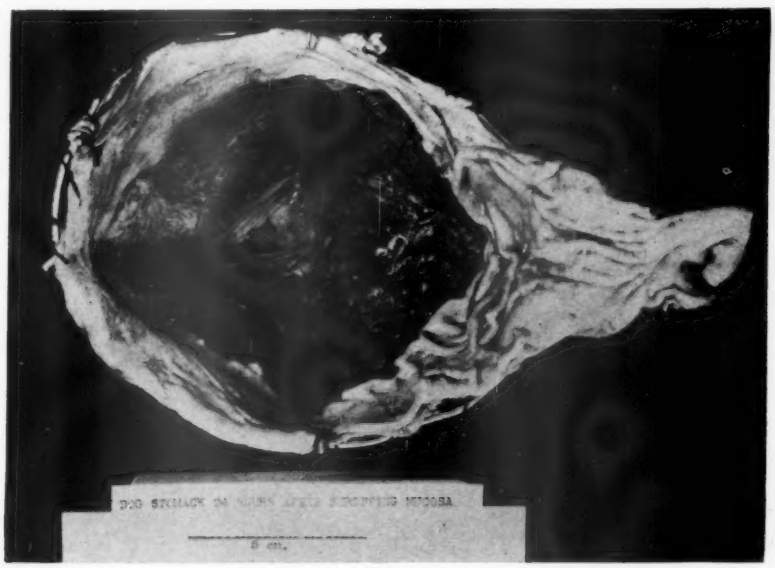

Fig. 1.—Gross specimen of dog stomach 24 hours after mucosal stripping, opened along lesser curvature. Mucosa of pyloric antrum and cardia, and along lesser curvature intact.

procedure.[1] Using the cat and dog as experimental animals, we have attempted in our laboratory to produce a complete alteration of regenerated mucosa by a 70 per cent to total excision of the gastric mucous membrane.

DOG EXPERIMENTS

Method.—Six healthy adult mongrel dogs were utilized for this study. They were operated on through longitudinal midline incisions while under endotracheal interrupted ether anesthesia. The stomach was delivered and opened through a 10 cm. incision made in the body of the organ in the longitudinal axis approximately 2 cm. from, and parallel to, the greater curvature. The mucosal layer was then stripped from all of the stomach except the area around the pyloric antrum, a small area around the cardia, and a 2 to 3 cm. strip along the lesser curvature which connected the two aforementioned areas (Fig. 1). With some difficulty, the tissue plane between mucosa and submucosa was developed by sharp and blunt dissection. Often we were able to remove the mucosa in

the fundic region by wiping it with a dry sponge but frequently had to use a sharp scraping dissection around the lesser curvature and prepyloric antrum. Bleeding was moderate but controlled by pressure. When completed, the gastrotomy wound was closed in two layers, using catgut on the inner row and interrupted fine silk sutures on the outer row. Whole blood transfusions of 100 to 200 c.c. were then administered through the femoral vein while the animal was still on the operating table. The animals were given nothing orally for from 24 to 48 hours. Fluids were replaced by parenteral administration. For the next week they were given, progressively, water with sucrose, diluted canned milk, milk-thinned Borden's meal (a proprietary bulk laboratory food), and finally regular Borden's meal. Prophylactic penicillin was given routinely for from 3 to 5 days.

Fig. 2.—Section of wall of dog's stomach immediately after mucosal stripping demonstrating residual glandular elements superficial to muscularis mucosae.

Preoperative histamine gastric . lyses were done in 5 of the 6 animals. Following surgery, histamine gastric analyses were repeated at various intervals, the gastric juice being obtained in the fasting animal through a Levine tube passed into the stomach. For the average-sized animal, 0.5 mg. of histamine was given subcutaneously 20 or 30 minutes before aspiration of the stomach. The gastric juice was examined for free and total acidity, and in some instances pH determinations were made on the Beckman pH meter.

Fig. 3.

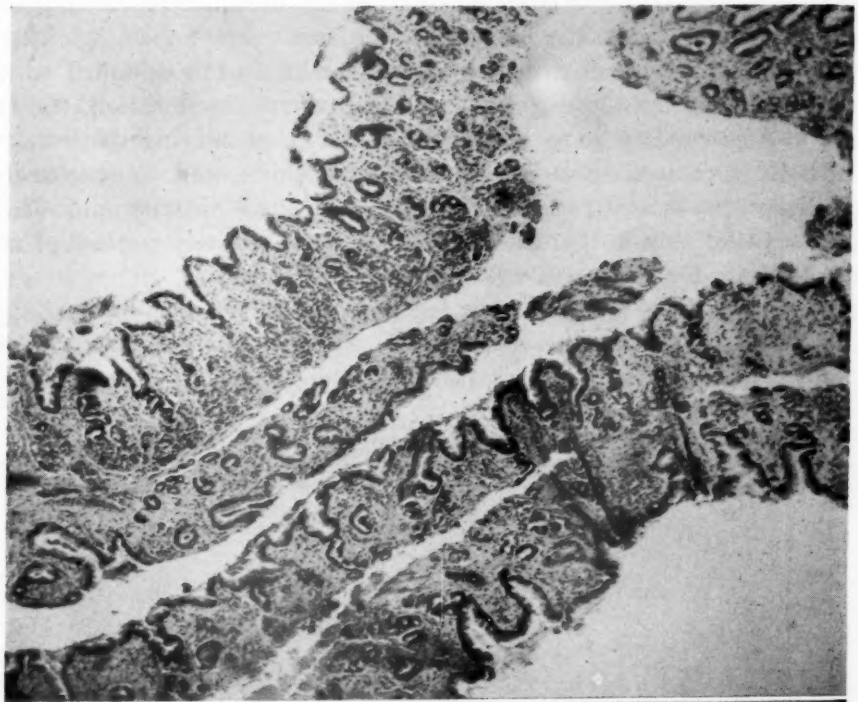

Fig. 4.

Fig. 3.—Section demonstrating coiled strips of mucosa removed from stomach of dog. Note level of separation and absence of muscularis mucosae.

Fig. 4.—Section showing microscopic appearance of wall of stomach of dog 2 weeks after mucosal stripping. Note dipping down of surface epithelium and early glandular formation.

Examination and biopsy of the regenerating mucous membrane were done by gastroscopy through an esophagoscope and by direct surgical approach at various intervals following the original procedure.

In two preliminary groups of experiments which were designed to remove large areas of mucosa in the dog and cat and prevent regeneration, the mucous membrane and submucosa were removed together, thus leaving the bare muscularis. In both instances, extensive scarring, thickening, and contracture of the gastric wall developed and resulted in complete gastric obstruction. This type of reaction was not seen in the dog when the more superficial method of mucosal stripping, described previously, was used.

Results.—Stripping of from 70 to 90 per cent of the gastric mucous membrane was accomplished relatively easily in the dog. In the present series of animals the mucosa was found to be particularly adherent along the lesser

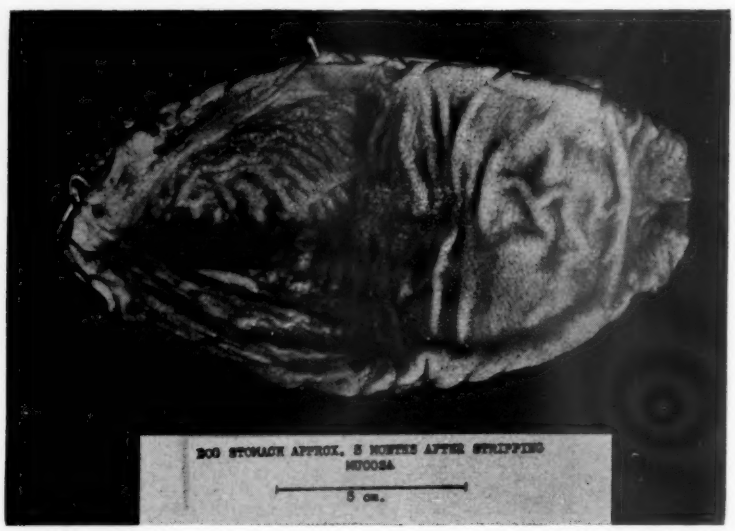

Fig. 5.—Gross specimen of dog stomach approximately 5 months after mucosal stripping. Note healed gastrotomy wound in center and complete regeneration of mucosa without scarring.

curvature and pyloric antrum. It was found that even with utmost care, complete removal of the deepest glands in the crypts was not feasible in the dog by the technique described. In most cases, a patchy, fine, velvety residue was left behind on the stomach wall. This residual material was identified by microscopic examination as glandular tissue from the bases of the foveolae. With some exceptions, the plane of separation passed superficially to the muscularis mucosae which remained more or less intact (Figs. 2 and 3).

Four days after stripping the mucosa, gastroscopic examination revealed the operative area to be bright red and glistening and quite friable. Biopsy of this area revealed some regeneration in what appeared to be a pre-existing, injured glandular pattern. Very bizarre cells, frequent mitoses, and a liberal piling up of epithelium were noted. On the tenth postoperative day, the gross appearance through the esophagoscope was not greatly altered. Granulation tissue predominated, and a nonspecific inflammatory reaction and an occasional

patch of regenerating mucosal cells were seen (Fig. 4). On the twenty-first postoperative day, the mucosa appeared almost normal except for an apparent lack of folds. Microscopic examination of the biopsy suggested normal mucous membrane. At the end of 11 weeks, the gastroscopic picture could not be differentiated from that of a normal stomach. This observation was borne out in the microscopic examination. At 3½, 4, 4½, 5, and 8 months after operation, surgical exploration revealed completely regenerated mucous membrane, which was essentially normal in gross appearance (Fig. 5). Some irregularity in mucosal folds was seen and, in one instance, a fine, velvety, "cobblestone" pattern was noted in the mucosa at the distal end of the regenerated area. A moderate irregularity of glands was noted microscopically, but a normal distribution and variety of cells were observed. Parietal cells were abundant. Regeneration was suggested in some areas by the apparent youth of the cells and their

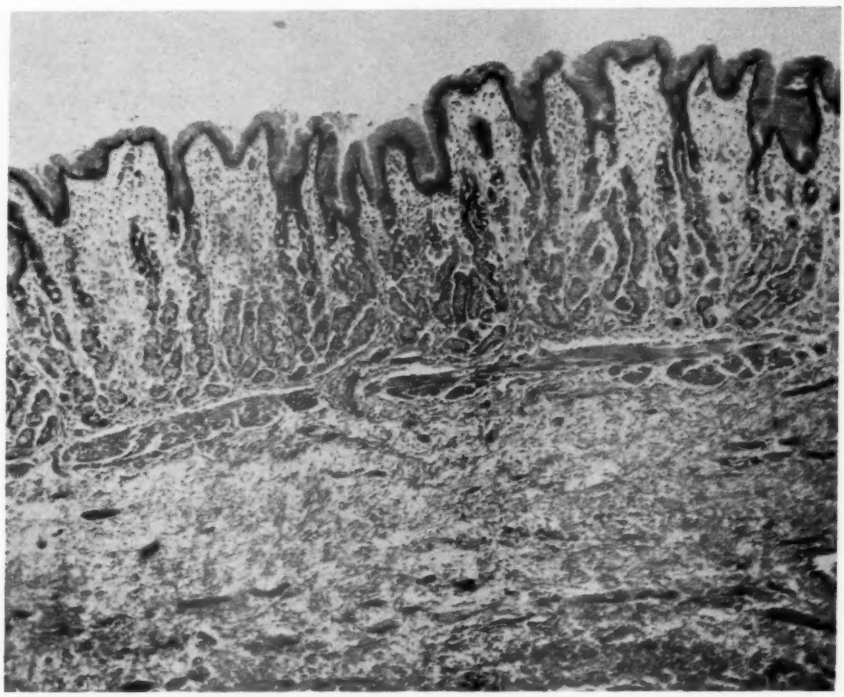

Fig. 6.—Section demonstrating completely regenerated mucous membrane 3½ months after mucosal stripping. Glandular elements essentially normal.

tendency to be less crowded but, by most criteria, the appearance was essentially normal (Fig. 6). It is of interest that scarification was not observed except along the line of the healed gastrotomy wound.

Gastric acidity: It was felt that because of technical difficulty, the method described above for obtaining gastric juices did not warrant more than gross observations regarding alteration in gastric secretion. A more critical investigation of all components of the gastric juice under similar conditions, utilizing the gastric pouch technique, is under way at the present time. It is pertinent to mention, however, that oral-gastric intubation in the dog may not be a very satisfactory or consistent method of obtaining gastric juice for analytic study.

Before operation all of the animals examined secreted adequate amounts of free hydrochloric acid in response to histamine. After operation this was also the case. However, the postoperative results were characterized by their inconsistency. Values varied erratically from day to day in the same animal and from one animal to the other. Generally, postoperative values were somewhat depressed. On some occasions, however, the sampling contained a greater amount of free acid than was the case preoperatively.

CAT EXPERIMENTS

Method.—Two procedures were employed in healthy, adult cats. In one series of 6 animals, an area approximately 6 cm. in diameter in the corpus of the stomach was stripped of its mucosa. In a second group of 9 animals, the entire gastric mucosa was removed and in 7 of these a gastrojejunostomy performed.

Fig. 7.—Cat stomach 74 days after stripping. Section suggests spreading of gastric mucosa from intact edge rather than regeneration from retained glandular elements in denuded area.

Animals in both series either died or were sacrificed at various intervals after the operation, the longest period of survival being 74 days. Biopsies were taken from representative areas of the stomach for microscopic examination.

Results.—Although the level of stripping was grossly the same in both the dog and cat, sections obtained from the cat stomachs one or two days after operation revealed no residual gastric glands in the denuded areas. The line

of separation appeared to be just at the level of the muscularis mucosae, which was left intact. The stomachs of animals surviving 10 days or longer revealed various stages of re-epithelization. The survival period extended from 10 to 74 days. In the first series of experiments, marked contracture of the size of the defect occurred with ingrowth of gastric mucosa about the periphery. In one instance, the defect was entirely healed and appeared relatively normal when examined grossly and microscopically 51 days after operation. In others, ulcers persisted as long as 44 days after operation. In the second series, where total extirpation of the gastric mucosa was done, only the 7 animals that had gastrojejunostomies performed at the same time survived the procedure for more than a week. The other 2 animals died of perforation of the stomach with generalized peritonitis. In all of the animals a marked contracture of the entire stomach wall with associated diminution of gastric capacity was noted. The pylorus was remarkably scarred and obstructed so that all of the drainage of the stomach occurred at the gastroenterostomy. This condition would explain the perforation which took place in the two animals that did not have a complementary gastrojejunostomy. Gross examination of the specimens suggested a slight ingrowth of the jejunal mucosa about the gastrojejunostomy stomas, and in 1 animal, followed for 74 days, there was a suggestion of irregular regeneration from the free margins of the gastric mucosa at the prepyloric and cardiac areas (Fig. 7). It was difficult to evaluate the degree of such extension in these specimens because of the extreme contracture, thickening, and scarring of the stomach wall.

DISCUSSION

The mechanism of regeneration of gastric mucosa has been the subject of many investigations during the past century. Its particular importance to the study of gastric ulcer need not be emphasized. In 1863, Pavy[5] produced a mucosal defect in the stomach of a dog and observed that it healed almost completely in 10 days. Subsequently, many other investigators used various techniques and made similar observations in both ulcer-bearing and nonulcer-bearing subjects. Early in this work, it became apparent that a distinction between erosion and ulceration must be made. This distinction had significant bearing on the problem inasmuch as it was shown that an erosion healed by epithelial proliferation without scar formation while an ulcer healed by granulation and scarification. According to Ivy and his associates[6] and Bockus,[7] the depth of the defect, not its size, is the differential factor between these two lesions. If a lesion does not penetrate the entire thickness of mucous membrane and the muscularis mucosae is intact, it is an erosion; if it penetrates the muscularis mucosae, the lesion heals by granulation and scarification and is considered an ulcer.

Arey[8] states that internal wounds of the serous and mucous surfaces differ in no fundamental way from those of the external surface. Periods of latency, fibroplasia, contraction, epithelization, and cicatrization are observed. The rate of repair is dependent upon the size and depth of the lesion, certain environmental factors relative to location, and various systemic factors which have been

thoroughly enunciated. Contraction of young connective tissue has been demonstrated to play a most important part in the reduction of the size of a defect of ulcer depth which must be covered by epithelium. In such cases the mucous membrane will not cover an area much larger than 1½ or 2 cm. in diameter by its own devices.[6]

Small erosions of mucous membrane will heal in relatively short periods of time. Residual gastric epithelium regenerates at a rapid rate and covers the defect without scarring. If these defects extend to the muscularis mucosae, they will usually epithelize in two or three days.[6] However, in the case of large defects, residual glandular elements must be present even though the muscularis mucosae is intact if regeneration of a normal mucous membrane is to occur without scarring. Small acute ulcers will usually be healed in less than 30 days. Defects as large as 5 cm. in diameter have been observed to be completely repaired in six weeks[4]; others, up to 8 cm., have taken as long as seven months.[9] The rate of repair in such cases is much more variable than in smaller defects.

In our series of dogs, when complete re-epithelization of from 70 to 90 per cent of the gastric mucosa was noted to occur in 3 weeks, it was apparent that: (1) total destruction of the gastric mucosa had not been accomplished, and (2) regeneration from residual glandular elements was taking place. Microscopic examination revealed that the muscularis mucosae was intact, as were the bases of many crypts from which regeneration had occurred so rapidly. In effect, mucosal stripping in the dog by this technique consists of making an extensive erosion of the mucous membrane. The mechanism of regeneration under these conditions is much the same as that described for smaller defects of this depth. The response is rapid, and the number, distribution, and types of regenerated cells are quite normal. These findings support the observations of others regarding the common origin of the various cells in the combined mucosa of the stomach.

Although the technique that was employed in the cats for stripping the mucosa was entirely comparable to that utilized in the dog, residual glandular elements were not found in the gastric wall. Healing proceeded in a manner characteristic of lesions of ulcer depth. There was marked contraction of the lesion with limited epithelial proliferation from the edges of the defect. In the animals that were followed for as long as 51 days, defects 6 cm. in diameter were noted to be completely re-epithelized.

It has been of interest to speculate how the results obtained by this study might be utilized in the human being. It has occurred to the authors that if the stripping could be performed at a level comparable to that employed in the dog, thereby leaving intact the glandular remnants from which rapid regeneration might occur, then hypertrophic gastritis, gastric polyposis, and possibly pyloric prolapsus of the antral mucous membrane might be managed satisfactorily by this technique, which would provide a method for preserving the gastric reservoir. Preliminary observations regarding this possible application have revealed that this technique of mucosal stripping, when employed in the normal

human stomach, completely denudes the muscularis mucosae of glandular elements in much the same manner as it does in the cat. Therefore, further observations in the human being are indicated before attempting to apply this technique clinically.

SUMMARY

As a means of alteration of the gastric mucosa for the purpose of reducing acidity, it is apparent that the technique of mucosal stripping as employed in these experiments does not produce sufficient injury in the dog to prevent the residual mucosa from regenerating a new, essentially normal, acid-producing mucous membrane. In the cat, such a technique produces marked alteration in the character of the gastric wall and mucosa, the major features of which are contraction and scarification. It is felt that the difference in response of the cats to the same procedure employed in the dog is due to a difference between the anatomic patterns of the stomach wall in the two species. In the dog, complete re-epithelization occurs by regeneration from the residual glandular elements left intact after stripping; whereas, in the cat, the absence of residual glandular elements in the wall precludes this reaction and invokes in its stead contraction, granulation, peripheral epithelization, and scarification.

ADDENDUM

In additional microscopic sections of the stomach wall, invasion of the musculature by malignant cells was found. Four weeks after operation hematemesis occurred and roentgenograms of the stomach taken after the ingestion of barium demonstrated constriction of the stomach in the area that had been denuded of mucosa. Total gastrectomy was performed Feb. 21, 1952, four weeks after the original operation. The denuded area had decreased 50 per cent in size, and there was no evidence grossly or microscopically of mucosal regeneration in this area.

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DISCUSSION

DR. WILLIAM P. LONGMIRE, JR.—Dr. Ravitch, if I may have the privilege, I would like to discuss one case in which partial removal of the gastric mucosa has been employed.

We did not wish to include this discussion in our paper as it represents only limited and very early observations. The patient was a 72-year-old man with giant hypertrophic gastritis. The lesion in this particular patient was quite typical of that previously described and was largely confined to the proximal three-fourths of the stomach mucosa. The mucosa of the pyloric antrum was essentially normal. In this case it was not possible to develop any clean cleavage plane between the mucosa and the submucosa because of the extensive distortion of the gastric mucosa and the extensive scarring throughout the layers of the stomach wall. The mucosa was removed more or less piecemeal after controlling the main vascular supply of the stomach with noncrushing clamps.

(Slide.) This is a microscopic section of the mucosa. The marked distortion and round-cell infiltration of the gastric wall as well as an area of carcinoma in situ may be seen. At operation, an additional biopsy of the musculature of the stomach wall was taken from an area in which invasion by malignant cells was suspected. No evidence of infiltration of the carcinoma into the deeper layers of the stomach wall was found. Two and one-half weeks have elapsed since the operation. The patient's diet has been steadily increased; he is now taking a regular diet and seems to have a fairly normal gastric capacity. We are extremely anxious to have a chance to observe any possible signs of regeneration of the mucosa in this area. It is our hope in this case that, with the marked distortion of the mucosa of the stomach, it will be possible in this particular type of disease process to strip off the top layers of the mucosa and leave enough remnant of gastric gland so that regeneration of a normal mucous membrane may occur.

GASTROINTESTINAL HEMORRHAGE AND ULCERATION ASSOCIATED WITH INTRACRANIAL LESIONS

A Clinical and Experimental Study

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GASTROINTESTINAL complications in patients with intracranial lesions are sufficiently common that they should be quickly recognized when they occur. Two such complications may be gastrointestinal hemorrhage,[1, 2, 9, 29, 33-36, 39] and/or ulceration.[9, 10, 13, 17, 24, 33, 34, 39] These changes may be chronically protracted, but are, in most instances, acute.

Our interest in this matter was stimulated by a recent series of patients who developed massive gastrointestinal hemorrhage after craniotomy for tumor. In reviewing our records, we were able to find seventeen cases in which such hemorrhage or hemorrhagic erosion and ulceration were associated with intracranial disease. However, the frequency with which these lesions are encountered at the autopsy table in patients with intracranial disease suggests that the incidence of such complications is much higher than these examples would indicate. Hart[14] observed that 17 per cent of ulcers disclosed at autopsy were associated with intracranial pathology.

Of additional interest in connection with these patients are the indications they may give concerning the disturbances in physiologic function which result in the formation of these gastrointestinal lesions. The fact that two distinctly different types of lesions were observed in the cases (ulceration or hemorrhage) indicates that different anatomic areas are involved. For this reason, a series of animal experiments was undertaken, similar to many reported in the past, in order to study the production of such acute gastrointestinal changes in their pure form.

The results of the clinical observations indicate that lesions so situated as to produce an imbalance in autonomic function by involving the hypothalamus or its afferent or efferent connections predispose the organism to develop either ulceration or hemorrhage in the gastrointestinal tract, while the added stress of operation, illness, or injury precipitates the formation of such visceral lesions. The conditions under which these phenomena occur were reproduced in animals by the placement of small lesions in the hypothalamus. Protection against such visceral lesions in these animals could be effected by the use of autonomic blocking agents.

Read at the meeting of the Society of University Surgeons, Baltimore, Md., Feb. 7-9, 1952.

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TABLE I. TYPE OF GASTROINTESTINAL LESIONS IN PATIENTS WITH BRAIN DISTURBANCES

TYPE	REVIEWED LITERATURE	THIS SERIES
Erosive*	81	5
Hemorrhagic†	63	12

*Lesions described as erosive were considered to be those variously classified as malacia, gelatinous softening, ulceration, acute perforation or ante-mortem autolysis.

†When significant acute petechial hemorrhages or gross extravasation of blood was present, the lesions were classified as hemorrhagic.[1, 2, 6, 9, 13, 22, 24, 29, 33-36, 39]

TABLE II. LOCATION OF GASTROINTESTINAL LESIONS IN PATIENTS WITH BRAIN DISTURBANCES*

SITE	REVIEWED LITERATURE	THIS SERIES
Esophagus	6	1
Esophagus and stomach	7	
Stomach	66	9
Stomach and duodenum	2	2
Duodenum	28	
Esophagus, stomach and duodenum	1	1
Colon	2	1
Stomach and colon	0	3

*Six survivors with upper gastrointestinal hemorrhage, whose lesions were not verified by x-ray examination or gastroscopy, were included in the total of nine patients listed as having changes confined to the stomach.[1, 2, 6, 9, 13, 17, 22, 24, 33-36, 39]

TABLE III. SUMMARY OF PATIENTS SURVIVING GASTROINTESTINAL COMPLICATIONS

		INTRACRANIAL PATHOLOGY		GASTROINTESTINAL PATHOLOGY	
CASE	AGE	TYPE	LOCATION	TYPE	LOCATION
W. M.	55	Cyst	Cerebellum	Preop.; ucler Postop.; hemorrhage	Stomach (x-ray) Upper G. I.
D. D.*	12	Tumor	Cerebellum	Hemorrhage	Upper G. I. and colon
A. W.	27	Tumor	Frontal	Gastritis	Stomach (gastroscopy)
T. H.	54	Lobotomy	Frontal	Hemorrhage	Upper G. I.
P. M.	33	Thrombosis	Middle cerebral area	Hemorrhage	Upper G. I.
D. P.	15	Tumor	Pineal body	Hemorrhage	Upper G. I.
C. L.	41	Tumor	Anterior clinoid	Hemorrhage	Upper G. I.
C. F.	38	Injury	Brain stem	Hemorrhage	Upper G. I.
J. F.†	43	Tumor	Hypothalamus	Hemorrhage	Upper G. I.

*D. D. showed additionally gross blood per rectum.

†J. F. survived postoperative hemorrhage, but succumbed four months later to his intracranial disease. The source of hemorrhage was presumed to be in the upper gastrointestinal tract in cases so designated on the basis of old blood in aspirated stomach contents or melena.

CLINICAL OBSERVATIONS

Clinical observations were made on seventeen patients in whom the association of brain disturbance and gastrointestinal ulceration or hemorrhage occurred. The central nervous system was involved by tumor in eleven cases (all had craniotomy), operation (lobotomy) in one, injury in two, and cerebral vascular accident in three instances. The sites of central nervous system disturbances were frequently gross or multiple. (The main structures involved are recorded in Table VI.) For this reason it was not possible to correlate the area of involvement in the brain with the site or type of gastrointestinal disturbance except in a general way. All patients had evidence of gastrointestinal ulceration or hemorrhage within eight days of the acute central nervous system disturbance. The

gastrointestinal lesions were predominately hemorrhagic (Table I) and occurred mainly in the upper tract (Table II), although multiple lesions were frequent and the colon was involved in four instances. In three cases both hemorrhage and ulceration occurred.

Nine patients survived and recovered (Table III). In these cases, gastrointestinal hemorrhage was verified by hematemesis or aspiration of gastric contents, by melena, or by the passage of blood by rectum. Eight patients succumbed, and in all of these hemorrhage or ulceration was verified by autopsy (Table IV).

TABLE IV. SUMMARY OF PATIENTS NOT SURVIVING GASTROINTESTINAL COMPLICATIONS*

CASE	AGE	INTRACRANIAL PATHOLOGY		GASTROINTESTINAL PATHOLOGY	
		TYPE	LOCATION	TYPE	LOCATION
J. C.	2	Tumor	Cerebellum	Hemorrhagic erosion	Colon
M. E.	54	Hemorrhage	Diencephalon and brain stem	Petechial hemorrhages and hyperemia	Stomach, duodenum and colon
V. M.	32	Injury	Parietal lobe and brain stem	Mucosal softening and perforation	Esophagus and stomach
L. R.	52	Tumor	Temporal lobe and diencephalon	Hemorrhagic erosions	Stomach and colon
M. B.	55	Tumor	Diencephalon	Hemorrhagic erosions	Stomach and duodenum
C. B.	34	Tumor	Temporal lobe and diencephalon	Hemorrhagic erosions	Stomach and duodenum
R. E.	28	Tumor	Frontoparietal and diencephalon	Hyperemia and mucosal autolysis	Stomach
C. S.	51	Hemorrhage	Frontoparietal and basal ganglia	Ulceration	Esophagus, stomach and duodenum

*All lesions were verified by autopsy.

CASE EXAMPLES

Hemorrhage.—

1. *Operation for third ventricular tumor followed by hemorrhagic erosions in stomach and duodenum:* M. B., a 55-year-old man, had a large ectopic pinealoma removed from the anterior portion of the third ventricle on Dec. 17, 1949. Shortly after surgery, the patient voided 1,500 c.c. of urine in two hours. Two hours later he vomited large amounts of coffee-ground liquid and soon went into profound shock. Transfusions and other supportive measures failed to improve his condition, and he died on the second postoperative day.

At autopsy the stomach contained approximately 300 c.c. of black-brown liquid. Hemorrhagic erosions were noted in the fundus and pylorus of the stomach, and in the duodenum (Fig. 1, *B*). The right adrenal was surrounded by hemorrhage. In the brain, the third ventricle was filled with clotted blood. The hypothalamus, caudate nuclei, and the right internal capsule were completey destroyed by hemorrhage (Fig. 1, *A*).

2. *Resection clinoid meningioma followed by acute gastrointestinal hemorrhage; recovery:* C. L., a 41-year-old man, was operated on Dec. 19, 1950, for a large recurrent meningioma arising from the anterior clinoid. In order to expose the tumor completely, it was necessary to remove a portion of the right frontal lobe. Three hours after surgery the blood pressure was normal, but one hour later it could not be recorded. The patient's condition remained critical until twenty hours after surgery when over 1,000 c.c. of bloody fluid were aspirated from the stomach. The patient was given 2,000 c.c. of whole blood and large doses of vitamin K, and his condition improved dramatically. Gastric bleeding continued intermittently for twenty-four hours and then did not recur.

Ulceration.—

3. *Cerebral injury followed by acute perforation of lower esophagus and stomach:* V. M., a 32-year-old woman, was admitted to the hospital on Feb. 16, 1949, in a coma, after being struck by an automobile. She died forty-eight hours after admission without regaining consciousness.

At autopsy diffuse subarachnoid hemorrhage was found. The inferior portion of the left parietal lobe was completely destroyed by hemorrhage. There were multiple smaller areas of hemorrhage throughout the remainder of the brain and brain stem. The left pleural

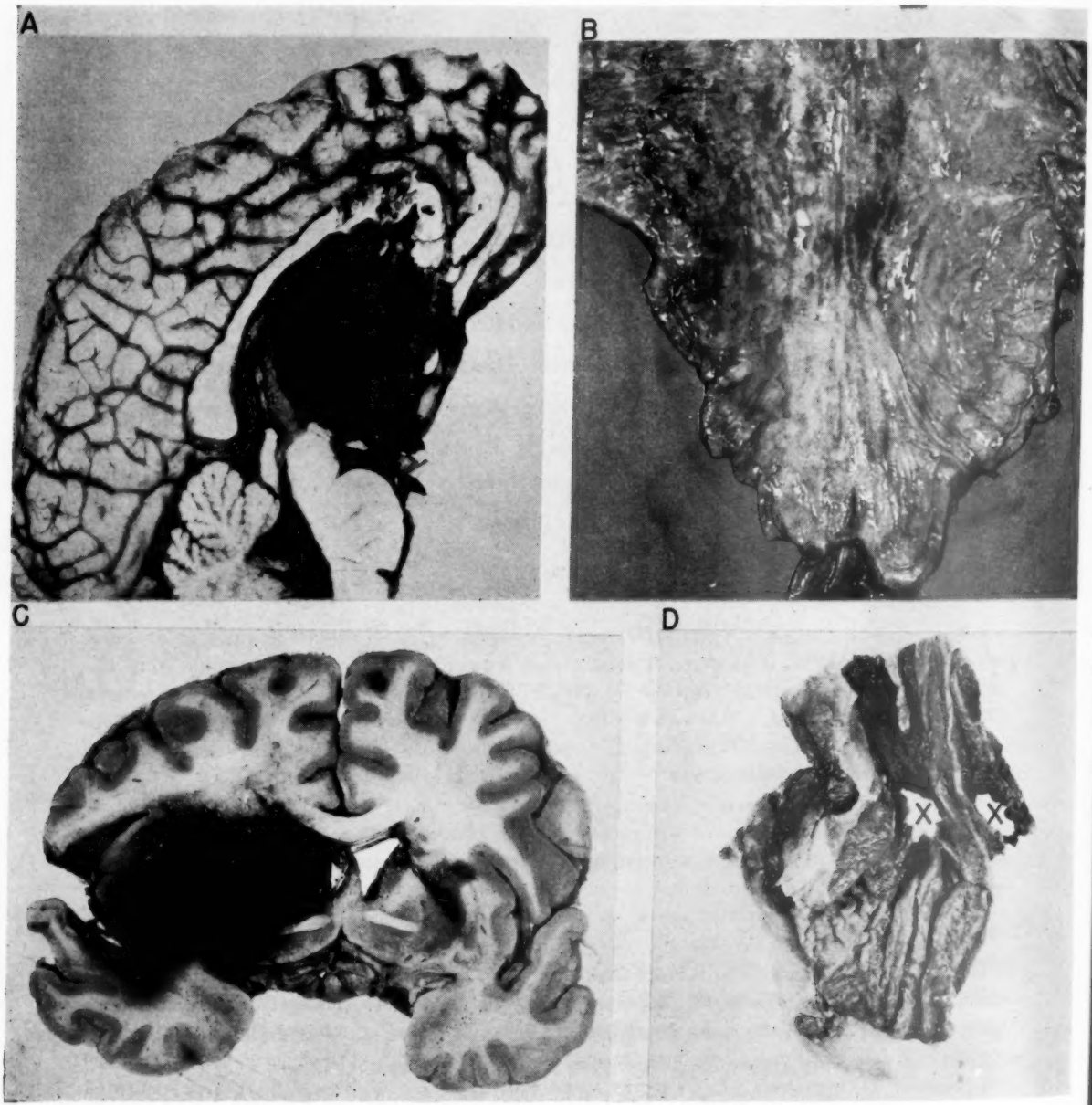

Fig. 1.—Photographs of brain lesions and gastrointestinal changes in patients. *A* shows the brain of patient M. B., while *B* shows multiple hemorrhages in the stomach of this patient. Hemorrhage in the brain of patient C. S. is shown in *C* while perforations in the lower esophagus are demonstrated (*X*) in *D*.

cavity contained a large amount of brownish liquid, in spite of the fact that there was no evidence of chest injury. The lower end of the esophagus and cardiac portion of the stomach were soft, thin, and necrotic. These changes did not appear to be the results of trauma. There was a large vertical perforation in the lower end of the esophagus through which gastric contents had escaped into the left pleural cavity.

4. *Cerebrovascular accident followed by acute perforation of gastric ulcer:* C. S., a 50-year-old man, had hypertension for fourteen years. Reportedly, he had hemorrhaged from the esophagus in 1937 and from a peptic ulcer in 1949. Shortly after the onset of a mild stroke in January, 1951, he vomited coffee-ground material, but recovered almost completely. A second, more severe stroke one month later was also associated with hemorrhage into the stomach and he succumbed after two weeks.

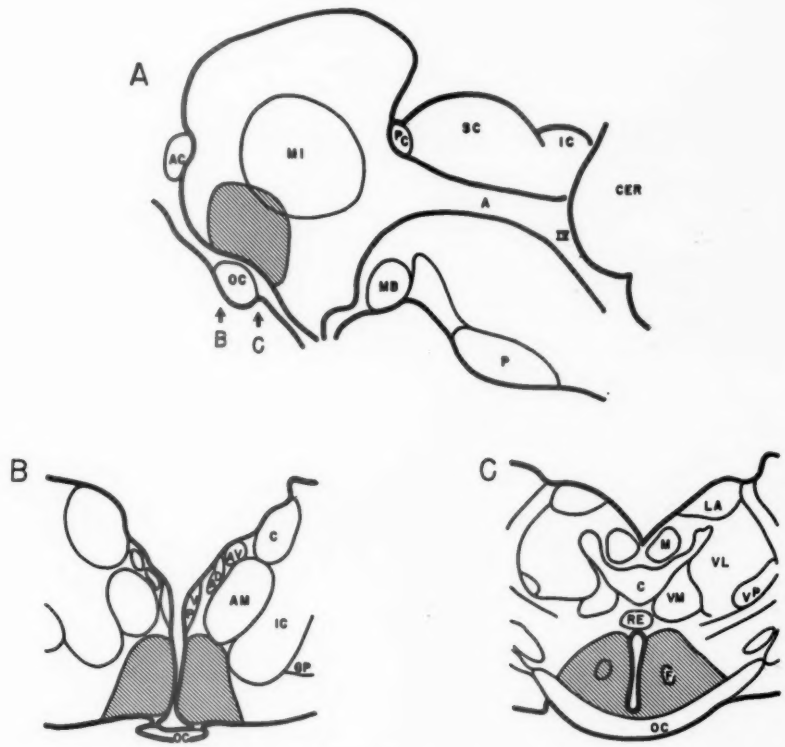

Fig. 2.—Anterior hypothalamic lesions.

At autopsy the brain showed a recent hemorrhage involving the left frontoparietal region and basal ganglia. Several areas of old softening were present in the right basal ganglia (Fig. 1, *C*). There were two large perforations of the esophagus near its entrance into the stomach from which about 400 c.c. of fluid had escaped into the left chest (Fig. 1, *D*). Several ulcer craters, measuring up to 3 mm. in diameter, were present in the stomach, and one, measuring 4 mm. in diameter, was visible on the posterior wall of the duodenum.

EXPERIMENTAL METHODS

Destructive hypothalamic lesions were made in a group of thirteen cats. Five lesions each were placed in the anterior (Fig. 2) or posterior (Fig. 3) hypothalamic regions, and three were centered in the tuberal area. Animals were anesthetized with sodium pentobarbital (35 mg. per kilogram), injected

subcutaneously. After craniotomy, the monopolar electrode was stereotactically oriented, and electrolytic lesions were made in the respective areas mentioned. Subcutaneous fluids and tube feedings were administered postoperatively as required. Animals were sacrificed after three weeks if they had not expired previously. After death, the entire gastrointestinal tract was thoroughly examined grossly, and microscopically when necessary; and the brains were kept for microscopic localization of the lesions.

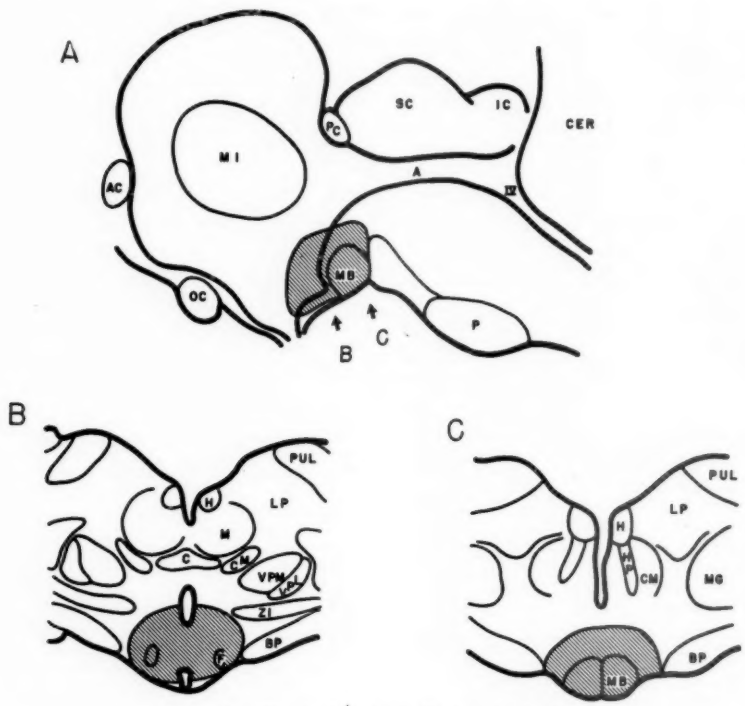

Fig. 3.—Posterior hypothalamic lesions.

In a second series of experiments, the effect of atropine and Etamon Chloride in preventing hemorrhage and ulceration induced by hypothalamic lesions was explored. Starting two days before operation, each of a group of three cats with anterior hypothalamic destruction was given atropine (1/3,000 gr. four times daily subcutaneously) and a similar group was given Etamon Chloride (15 mg. four times daily subcutaneously) which medications were continued until the animal expired. The results from these groups were compared with those of another group which had received no medication. A similar series of experiments was run with posterior hypothalamic preparations.

Gastrointestinal hemorrhages or ulcerations were found in twelve of the thirteen animals in the initial experiment. Of the five cats in which anterior hypothalamic lesions were made, four showed submucosal gastric hemorrhages. In the group with posterior hypothalamic lesions, four animals had pure gastric ulcers, and the fifth showed both hemorrhages and ulceration, although in different regions of the stomach. Two of the three animals whose lesions were

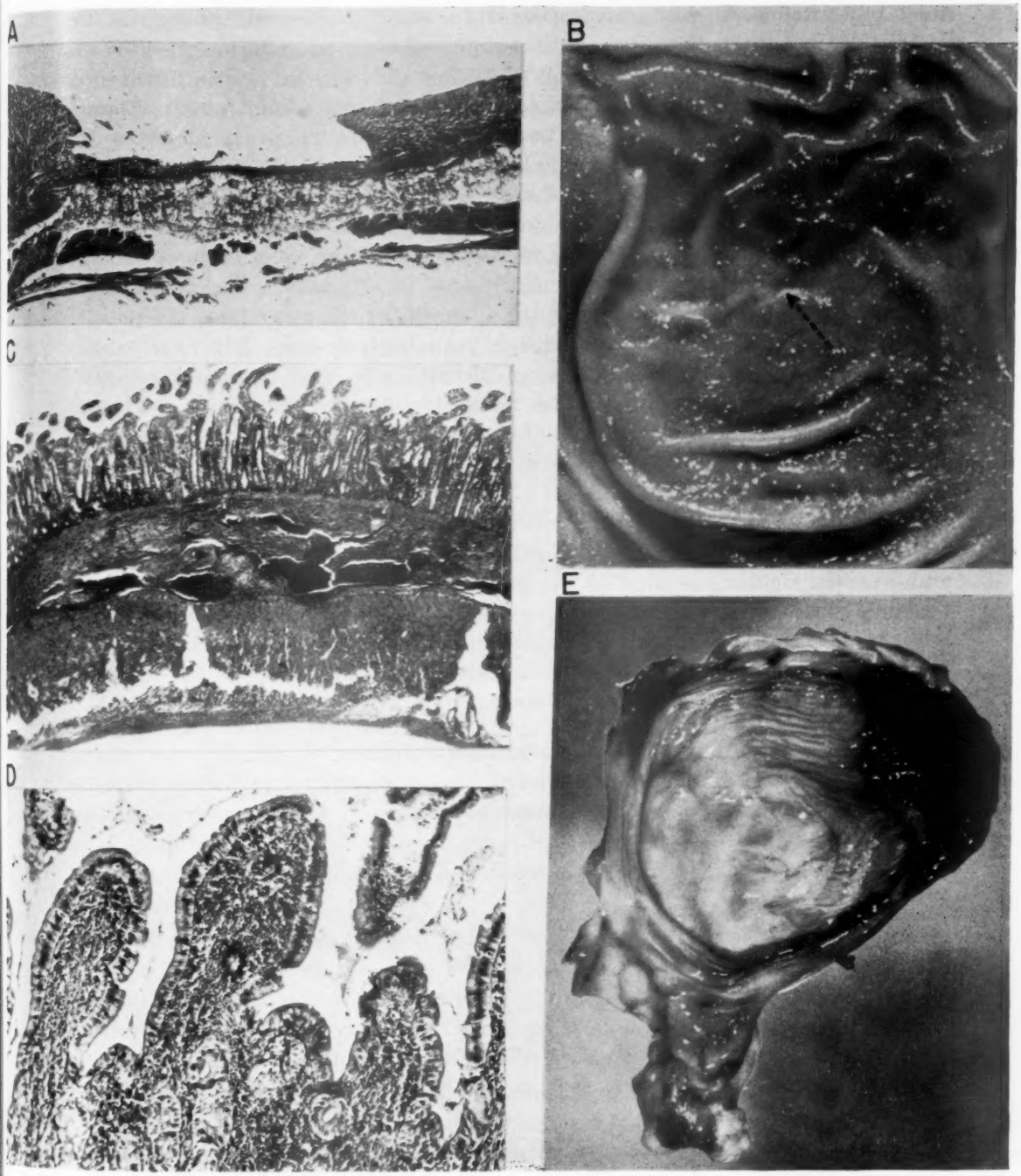

Fig. 4.—Microscopic (*A*) and gross (*B*) ulcerations (arrow) are shown in the stomach of cats with electrolytic lesions in the posterior hypothalamus. Submucosal (*C*) and mucosal (*D*) hemorrhages are apparent in photomicrographs of the small intestine and colon, respectively, of animals with lesions in the anterior hypothalamus, while hemorrhage in the stomach (*E*) can be seen grossly in a similar preparation.

in the tuberal area had both gastric ulceration and hemorrhage. The third such preparation showed only hemorrhages. In all cases, ulceration was confined to the stomach while hemorrhages frequently occurred throughout the gastrointestinal tract (Fig. 4).

The effectiveness of atropine and Etamon Chloride in preventing gastrointestinal lesions was apparent in animals where each was administered. Etamon Chloride completely prevented the production of hemorrhages in all three cats with lesions of the anterior hypothalamus, while those with similar areas of brain destruction which were treated with atropine showed petechial submucosal hemorrhages in the stomach of two animals and in the duodenum of the third. As noted, control animals receiving no medication after anterior hypothalamic lesions exhibited gastrointestinal hemorrhages in all cases. The hemorrhages occurred in the cecum of one and in the stomachs of the other two.

The three animals with posterior hypothalamic lesions that were treated with Etamon Chloride showed gastric ulceration in two cases. Atropinized animals, on the other hand, showed no gastrointestinal pathology. The untreated animals with posterior hypothalamic lesions, which served as the controls in this series, showed pure gastric ulceration in two cats and both ulceration and hemorrhage in the third.

The lesions in the brain were small and discrete in all cases involving various portions of the hypothalamus. Anterior lesions included the supraoptic, and paraventricular nuclei, and the general preoptic region. Posterior hypothalamic destruction was confined, for the most part, to the mammillary bodies and the posterior nuclei. In the three animals with lesions in the tuberal area, the ventromedian, dorsomedian, paraventricular, and part of the posterior nuclei were destroyed. The experimental data are summarized in Table V.

TABLE V. EXPERIMENTAL RESULTS

LESIONS	MEDICATION	HEMORRHAGE	ULCER	HEMORRHAGE & ULCER	NO PATHOLOGY
Anterior hypothalamic	None	7			1
	Atropine	3			
	Etamon				3
Posterior hypothalamic	None		4	1	
	Atropine				3
	Etamon		2		1
Combined	None	1		2	

DISCUSSION

The cases reported here are summarized in Tables III and IV. The two types of acute gastrointestinal lesions, which have been frequently reported by other observers, were seen. One type of lesion was characterized by gross hemorrhage or diffuse petechiae. The other change was manifested by gelatinous softening, erosion, or perforation, as originally described by Rokitansky,[30] in 1855. Our experience regarding the incidence of these two pathologic processes is at variance with that apparent in a random review of 144 reported cases (Table I) in that hemorrhagic changes predominated in this series.

The specific structures in the central nervous system, injury to which resulted in these gastrointestinal lesions, are somewhat difficult to determine pathologically because the brain disorders are usually gross or multiple. Animal experimentation, however, has indicated a relationship between disturbances in the autonomic centers of the brain and the changes which occur in the gastrointestinal tract.[8, 16, 18, 31] Table VI demonstrates that in approximately half of all clinical cases, the pathological process of the brain involves the hypothalamus and, in most of the remaining instances, is in a position to interfere with its known centripetal connections from the frontal lobe or centrifugal pathways in the brain stem or medulla oblongata. The few remaining lesions may have caused functional disturbance of the diencephalon by producing edema, although the case of Wyatt and Khoo,[39] in which a small hemorrhage involved the cortex of the Island of Reil, is quite interesting when correlated with investigations indicating mediation of certain autonomic function by this area. There was no correlation between the type of brain lesion which existed and gastrointestinal abnormalities produced.

TABLE VI. LOCATION OF BRAIN LESIONS ASSOCIATED WITH GASTROINTESTINAL DISTURBANCES*

SITE OF BRAIN LESION	REVIEWED LITERATURE	THIS SERIES
Frontal lobes exclusively	4	2
Hemispheres elsewhere	5	2
Diencephalon involved	32	8
Brain stem	6	2
Cerebellum	9	3

*These subdivisions were established to permit tabulation of frequently diffuse brain lesions for evaluation of areas most often involved in patients with gastrointestinal disturbances. Cases in the reviewed literature were included only when location of the abnormality was accurately described.[1, 2, 9, 13, 17, 22, 24, 25, 34-36, 39]

The gastrointestinal changes appear to be located predominantly in the upper tract (Table II), although less exclusively so in our series than in those reported elsewhere. Thus, we found disturbances in the colon in four of seventeen cases, whereas such changes were reported only twice in 112 cases reviewed at random in other series. The stomach was most frequently involved, but the lesions were commonly multiple and were often found in several parts of the gastrointestinal tract.

Age appeared to exert no influence on the association of brain and gastrointestinal lesions. The youngest patient in our series was two years old and the oldest was fifty-five. Only one of the seventeen patients was a woman, although the group was somewhat selective in that eleven of the patients were observed in the Veterans Hospital. This sex differentiation may have some significance, however, in view of the fact that chronic ulcer is predominantly a disease of men.

Only two of the seventeen patients had gastrointestinal symptoms before hospitalization (W. M. and A. W.) and one of these had severe hemorrhage from the stomach after operation. In the remaining fifteen cases, the gastrointestinal manifestations were first noted from a few hours to eight days after operation, accident, or other acute cerebral insult. Nine patients survived, and in none of these were there persistent or recurrent gastrointestinal disturbances.

Existing experimental evidence parallels and, to some degree, clarifies the clinical manifestations of gastrointestinal disturbances in patients with brain lesions. Both erosive and hemorrhagic processes have been observed in animals following the injection of Pitressin,[6, 26-28] acetylcholine,[26] pilocarpine,[23] ephedrine,[38] and histamine.[15] Such changes have been variously imputed to vasospasm, stasis, anoxia from contraction of the gut wall, and increased gastric secretion.

Reported stimulation and destruction experiments suggest a possible basis for the occurrence of the apparently different ulcerative and hemorrhagic lesions in the gastrointestinal tract (Tables VII and VIII). In general, sympathetic responses (diminished motility) were observed on stimulation of the orbital cortex[3] and of the posterior hypothalamus,[5] while vagotonic or parasympathetic reactions were noted on stimulation of the anterior hypothalamus[4, 37] and brain stem.[32] Correspondingly, destructive lesions of the anterior hypothalamus have produced hemorrhagic erosions (protected by sympathectomy)[19] and of the more posterior parts of the hypothalamus crater formation (protected by vagotomy).[19, 20] Both hemorrhagic[7] and ulcerative[12] changes in the gastrointestinal tract have been described following lesions in the brain stem.

TABLE VII. EFFECTS OF EXPERIMENTAL STIMULATION OF THE NERVOUS SYSTEM ON THE GASTROINTESTINAL TRACT: SUMMARY OF PUBLISHED DATA

SITE OF STIMULATION	GASTROINTESTINAL RESPONSE	REMARKS
Orbital surface, frontal lobes	Diminished tonus[3]	
Anterior hypothalamus	Increased motility[4, 5, 37]; blanching	Blocked by section of vagi
Posterior hypothalamus	Obliteration of motility[4, 5]; fall of intragastric pressure	
Brain stem	Increased motility[32]	Blocked by section of vagi
Vagi	Increased motility[4]; short latency	
Splanchnic	Contraction of vessels of stomach[32]	

The evidence available in the experimental animals here reported is in direct agreement with these data. Mucosal and submucosal hemorrhages predominately in the stomach, but frequently in the rest of the gastrointestinal tract, could be produced with surprising regularity by lesions made in the anterior hypothalamus. The posterior hypothalamus, subserving sympathetic

TABLE VIII. EFFECTS OF EXPERIMENTAL DESTRUCTIVE LESIONS OF THE NERVOUS SYSTEM ON THE GASTROINTESTINAL TRACT: SUMMARY OF PUBLISHED DATA

SITE OF DESTRUCTIVE LESION	TYPE OF G. I. LESION	LOCATION OF G. I. LESION	REMARKS
Hemispheres	None[16]		
Anterior hypothalamus	Hemorrhagic erosion[16]	Stomach[16] Colon[18]	Protected by sympathectomy but not vagotomy[20, 21]
Posterior hypothalamus	Crater formation[19]	Stomach[20] Duodenum[20]	Protected by vagotomy but not sympathectomy[20, 21]
Brain stem	Ulceration,[12] hemorrhage[7]	Stomach[12] Stomach[7]	
Vagi (stress added)	Hemorrhagic erosion[20]		Not protected by sympathectomy
Splanchnic nerves	None[20]		Hemorrhagic and nonhemorrhagic lesions

functions, was then unopposed and the hemorrhagic changes presumably resulted from this imbalance. That such is the case is suggested by the fact that these hemorrhages did not occur when the animals were protected by sympathetic blocking agents.

Conversely, pure erosions occurred when the lesions were placed in the posterior hypothalamus producing autonomic imbalance in favor of the vagotonic anterior nuclei. Again, such influences were rendered impotent in producing ulceration with parasympathetic and with general autonomic blocking agents. Unlike hemorrhagic lesions, erosions were limited in the animals largely to the stomach and it can only be supposed that digestive juices confined to this structure may play a vital role in the production of these changes. Tending to support such a conjecture is the fact that direct stimulation of the anterior hypothalamus results in prompt and excessive elevation of hydrochloric acid in the stomach.*

Thus, in animal experimentation and in clinical observation, both erosive and hemorrhagic disturbances have been observed in association with brain lesions. Certainly, these gastrointestinal changes are acute and rapid in their development and occur at times of sudden or severe incident. It appears, therefore, that the brain lesion, if properly situated, disrupts the balance of visceral function centrally mediated. The coincident severe stress of injury, illness, or operation superimposed on this imbalanced autonomic system may participate as a precipitating factor in the formation of these gastrointestinal lesions.

It would seem that homeostasis is rapidly re-established in nonfatal cases, however, in that none of the nine patients who survived had persistent or recurrent gastrointestinal symptoms. This factor makes recognition and prompt treatment of such complications in patients, who are frequently comatose, all the more pressing. One of our patients who succumbed might have survived had it been possible to prevent or control his hemorrhage, and two of the patients who recovered would not have done so but for the alertness of our house officers in establishing the diagnosis by gastric aspiration and in instituting prompt therapy. In three other survivors, the cause for a stormy convalescence was obscure until tarry stools were reported. Treatment in all cases has consisted of replacement therapy and of the administration of vitamin K. We had considered earlier, but had not used, the prophylactic or therapeutic injection of autonomic blocking agents. The protection afforded animals by such substances would warrant their trial.

It remains to be seen whether or not there is any connection between acute lesions of the type demonstrated in man and animals in this and other studies and chronic ulceration of the gastrointestinal tract. Certainly the latter condition is frequently encountered in central nervous system disturbances[34] and constant reference is made to the role of psychogenic factors in this connection. Should subsequent information substantiate this relationship, such data as these suggest the possibility at least that the initial process in chronic ulceration can be either erosive, due to parasympathetic predominance, or focally hemorrhagic,

*Porter, R. W.: Unpublished data.

due to sympatheticotonia. In either case, the chronic ulcerations so initiated might be identical due, presumably, to local factors indigenous in the gastrointestinal tract.

We are grateful for the assistance of Wilma Weeks and Cora Rucker in making the tissue preparations and of Timothy Dodge, Thomas Masterson, and Charles Bridgeman in preparing the figures.

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DISCUSSION

DR. H. WILLIAM SCOTT, JR.—This has been a most interesting and informative presentation. About twenty-odd years ago Dr. John Powers described his experiences with attempts at closure of perforated Cushing ulcers in, I believe, one or two cases. He encountered considerable difficulties because of the fact that, after closing these perforated ulcers, the closure subsequently sloughed and the patient died. Some six years ago, Dr. Frank Otenasek and I had a patient here at Hopkins with an infected cerebellar astrocytoma who developed a perforated Cushing ulcer. We operated on this patient and closed the perforated ulcer and did a simultaneous vagotomy with the hope that subsequent sloughing of the closed ulcer might be obviated. This patient survived the operative procedure and did not develop any further gastrointestinal difficulties but unfortunately died with meningitis about twelve days after closure of the ulcer. We were not able to obtain an autopsy. Consequently, it is difficult to draw many conclusions from this case but it was our opinion that the vagotomy may have been of value. If the neurological lesion which is responsible for the gastrointestinal ulceration is not inevitably fatal, it seems to me that the possibility of using either vagotomy or a chemical blocking agent, such as has been described, may offer some hope of success in the management of Cushing ulcers.

DR. FRENCH (Closing).—Thank you, Dr. Scott. I agree that such a procedure is entirely desirable. We have not yet tried the use of these blocking agents in neurosurgical patients because it doesn't seem justifiable to use them in all instances. However, it might be desirable to use some such blocking agent in those cases where operation is performed in the region of the diencephalon and third ventricle.

A CRITICAL EVALUATION OF THE BILLROTH I GASTRIC RESECTION

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INTRODUCTION

THERE are two general methods available for the re-establishment of gastrointestinal continuity after resection of the lower portion of the stomach. These methods involve utilization of either gastroduodenal anastomosis (Billroth I and its modifications) or gastrojejunal anastomosis (Billroth II and its modifications). The initial popularity of gastroduodenostomy after its first successful performance in 1881 by Billroth[2] was short-lived because of the discrepancy between the circumferences of the duodenum and stomach and because of the frequent leakage which occurred at the suture line.

Today many surgeons reject this procedure in favor of the more popular gastrojejunal anastomosis on the basis of this prejudice.[17] Other surgeons[5, 13] consider its scope of usefulness limited, for the most part, to those cases with no duodenal pathology.

Various modifications of the original Billroth I have been described[11, 16, 17, 25, 28] with the idea that they would make its utilization more widespread. By and large, with a few exceptions,[4, 5, 10, 13, 20] modern surgeons still prefer the Billroth II and its modifications.

There are certain physiologic mechanisms which are dependent on gastroduodenal continuity, which is the normal anatomic arrangement. Would it, then, not be preferable to maintain this arrangement insofar as it is feasible to do so?

It is, therefore, reasonable to seek a critical evaluation of this procedure, weighing the advantages against the disadvantages in the light of the technical feasibility of its performance. It is in the interest of such evaluation that this study was undertaken.

SELECTION OF CASES

The main section of this study includes 93 cases of gastroduodenal anastomosis following resection of a portion of the stomach performed at the King County Hospital in Seattle during the four-year period beginning Jan. 1, 1948. This portion of the series includes all of the Billroth I resections which have been performed at this hospital up to Jan. 1, 1952. The selection of cases for

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gastroduodenostomy in the King County Hospital series depended on two main factors: (1) the preference of the individual surgeon either for this procedure or for the Billroth II, and (2) whether the case was operated on early or late in the series. The first factor is of significance because the resections done by the authors or members of the service of the senior author were of the Billroth I type whenever possible, particularly since the beginning of 1950; however, many Billroth II operations by other surgeons at the hospital probably could have been of the Billroth I type had the preference obtained. The importance of the second factor in the selection of cases lies in the fact that with increasing experience with this procedure the technical feasibility of using gastroduodenostomy in cases with duodenal pathology has been progressively realized. During

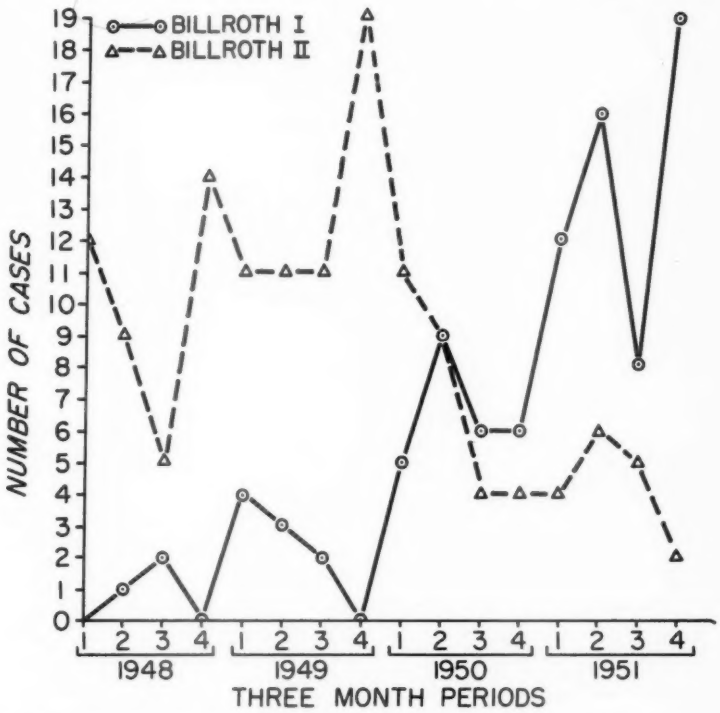

Fig. 1.—This shows the trend in our series at the King County Hospital of the frequency with which we have done the Billroth I (inclining line) and the Billroth II (declining line) respectively. It is noteworthy that six of the seven Billroth II's done in the last 6 month period of 1951 were done by surgeons other than ourselves, these surgeons having no particular preference for the Billroth I.

the last 3 months of this series we have been particularly impressed with the fact that we can broaden the scope of gastroduodenostomy by using the Von Haberer-Finney end-to-side modification in cases which would otherwise necessitate the use of the Billroth II. This has previously been stressed by Fallis and Barron[10] and Balfour.[1] In the last 3 months of the series we have used the end-to-side modification four times, whereas in the preceding 45 months we used it only twice. Eighty-eight per cent of these 93 cases were operated on by one or the other of us or on the service of the senior author.

With these facts in mind, reference is made to Figs. 1 and 2.

This study also includes 4 cases operated upon at other hospitals in 1951. Two were done by one of us (H. N. H.) and two were done by another member of the Department of Surgery of the University of Washington.

In addition, 7 cases operated upon in 1951 at another hospital are included from the private practice of Dr. Hilding H. Olson, a former resident from the service of the senior author. His criteria for using the Billroth I are identical with ours.

The 104 cases from these sources constitute the material for this study.

TECHNIQUE

The technique which we describe below is that employed by us at the present time. From time to time during the series we have modified our methods, but the following technique, in our hands, seems best at present.

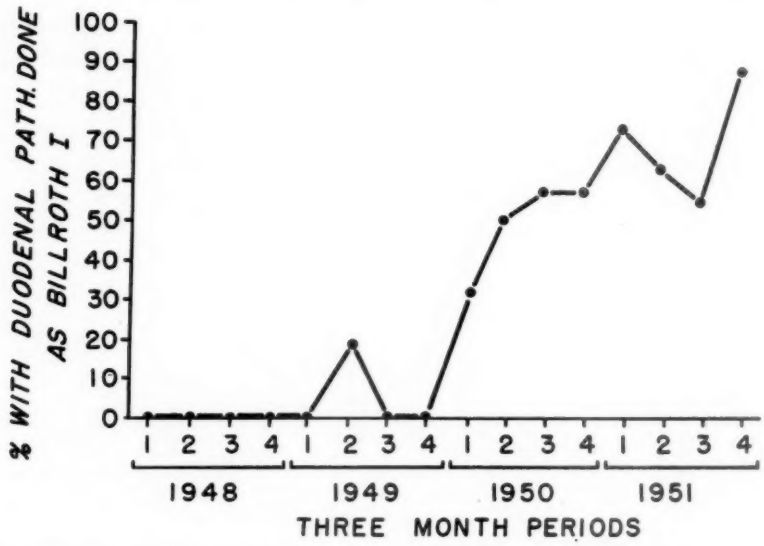

Fig. 2.—This shows the increasing proportion of patients with operations for duodenal ulcer which were of the Billroth I type at the King County Hospital.

General Principles

1. Interrupted silk sutures are used throughout except for the wound closure, for which we use steel wire.

2. The anastomosis is of the open type. For this we use two layers of interrupted silk.

3. No drainage is employed except in those cases where trauma to the pancreas occurs. In such instances we use either a Penrose drain or a double lumen, sump-suction catheter.

4. The final decision regarding the use of gastroduodenal anastomosis is not made *until after* an adequate resection has been performed. The anastomosis must be made without undue tension in normal tissue.

As previously emphasized by W. J. Mayo[17] and others[10, 22, 23] *the anastomosis should not be forced.*

Steps

The procedure may be outlined in the following ten steps:

1. *Incision and Exploration.*—An upper midline incision is made, beginning in the left xiphocostal angle and extending down to, or below, the umbilicus. The entire abdomen is explored including external observation of the gastric or duodenal pathology and the final decision to resect is made (Fig. 3, *a* and *b*).

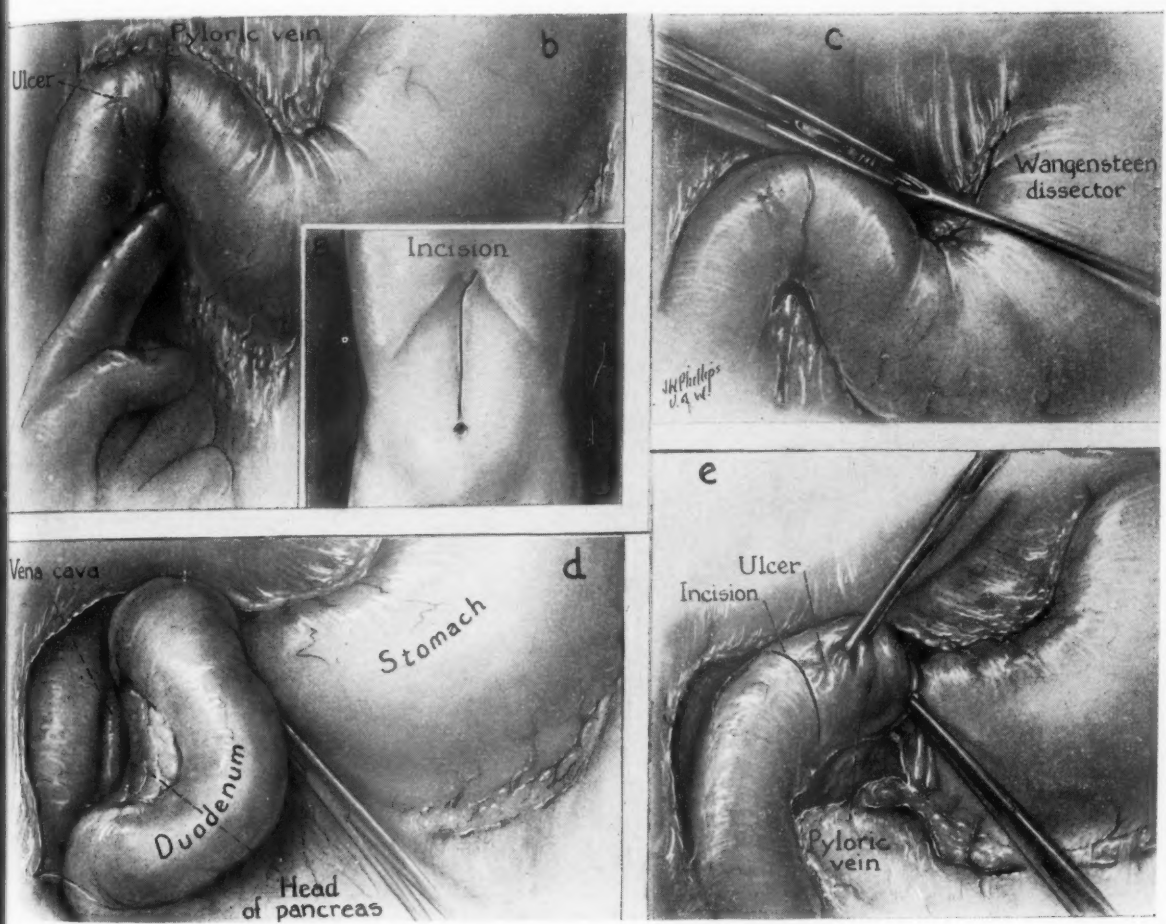

Fig. 3.—Techniques of Billroth I. Initial steps.

2. *Freeing of the Lower End of the Stomach.*—The gastrocolic and gastrohepatic omenta are freed from the lower 5 to 6 cm. of the stomach; the right gastric and right gastroepiploic vessels are usually ligated. A Penrose drain is placed about the freed lower portion of the stomach for ease in handling (Fig. 3, *c* and *e*).

3. *Mobilization of the Duodenum.*—The second and third parts of the duodenum are extensively mobilized after the method of Kocher.[16] The lateral peritoneal reflection off the retroperitoneal portion is incised, and then by blunt and sharp dissection the duodenum is mobilized and rotated on its long axis to

the left and superiorly as far distally as the superior mesenteric vessels. The head of the pancreas and the lower end of the common bile duct move with the duodenum as a unit, although maximal mobilization is achieved distal to these structures. This is essentially an avascular dissection. When fully mobilized, the following structures should be exposed: the right ureter, inferior vena cava, lower end of common bile duct, and occasionally the aorta. Unless most of these structures are visible, mobilization is incomplete (Fig. 3, *d*).

This maneuver not only facilitates gastroduodenal anastomosis, but it serves two other important functions: (1) it minimizes the chance of injury to the

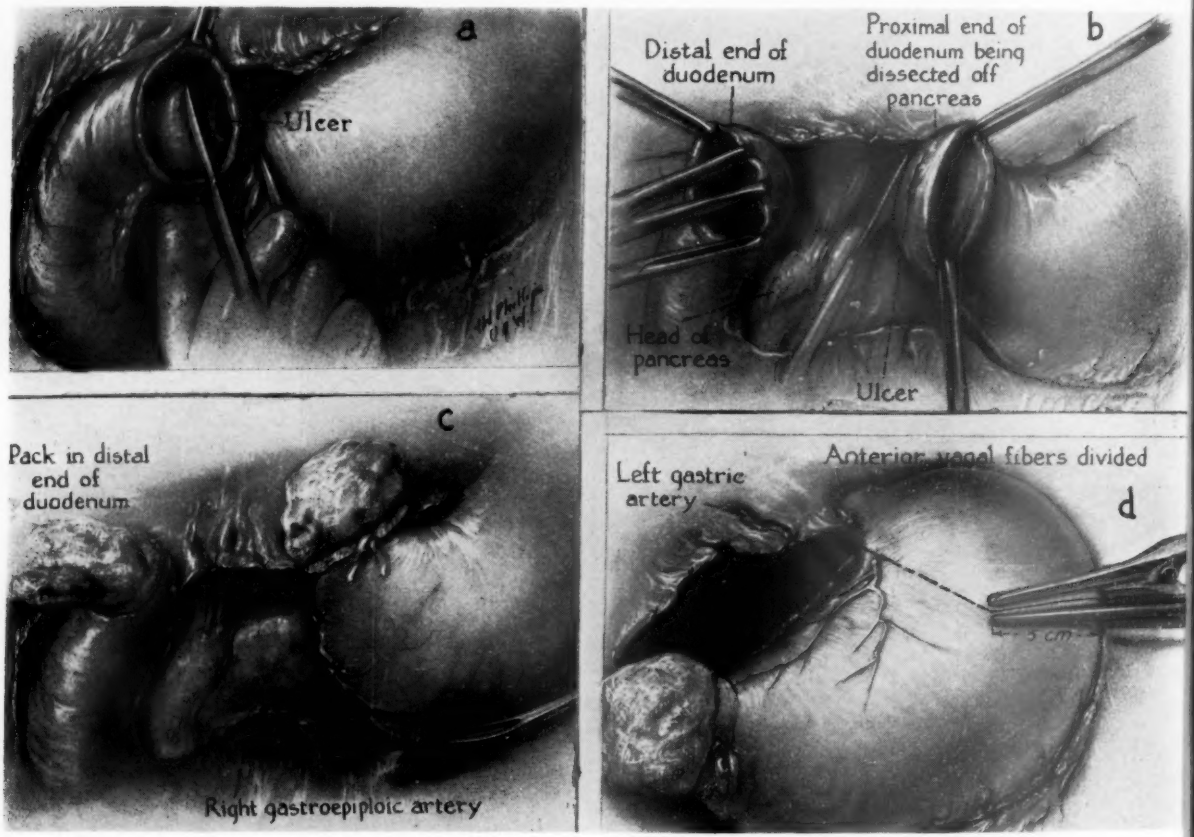

Fig. 4.—Techniques of Billroth I, continued.

common bile duct by better visualization, and (2) it allows the dissection about the proximal duodenum and its severance to be performed in a more superficial part of the operative field.

4. *Division of the Duodenum.*—When the ulcer is in the anterior duodenal wall or merely adherent to the pancreas, the duodenum is divided distally and the ulcer is removed. In the case of the posterior ulcer penetrating the head of the pancreas, the duodenum is sharply dissected from the ulcer bed from the right side by the method of Strauss to be described later. On occasion we leave the more distally located ulcers in place, undisturbed. Dr. Alfred A. Strauss[27] of the Michael Reese Hospital, Chicago, has demonstrated to us a very useful

maneuver in dividing the duodenum (Fig. 4, *a* and *b*). This consists of displacing the duodenum anteriorly with one finger while incising first the anterior wall and then the posterior wall from inside the lumen, both distal to the ulcer. No clamps are used on the duodenum. A sponge is placed in the lumen of the duodenum which is left until after the resection has been completed (Fig. 4, *c*).

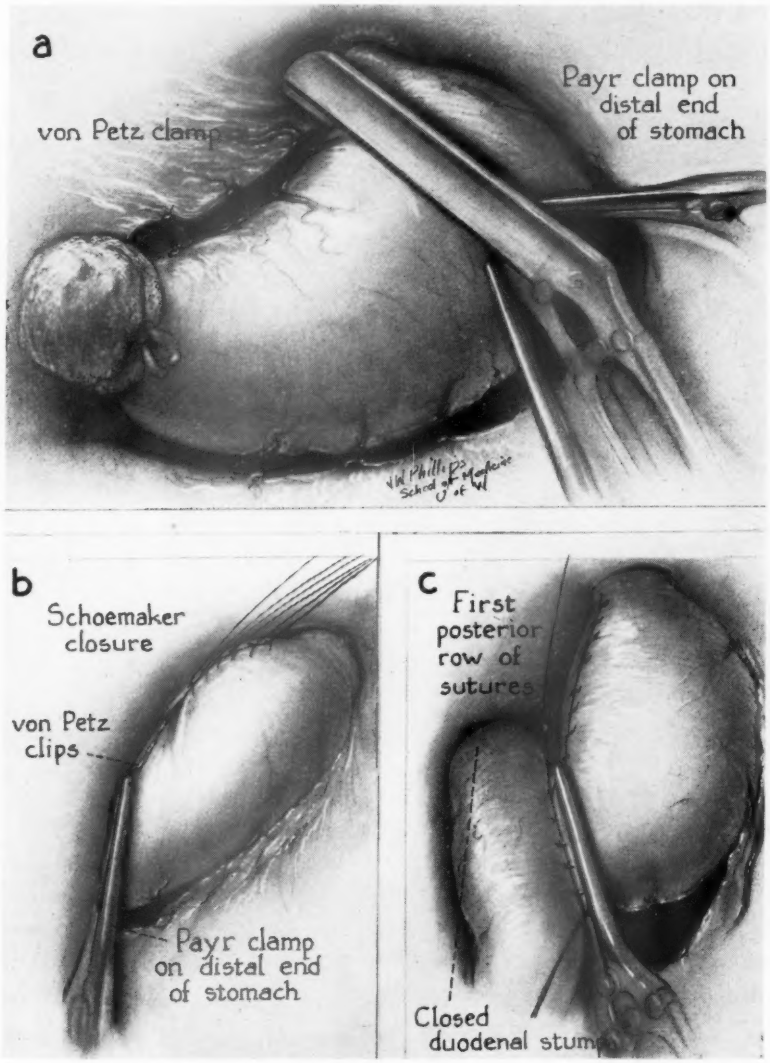

Fig. 5.—Techniques of Billroth I, continued.

5. *Freeing of the Greater Curvature.*—The greater curvature is freed up to, but usually not including, the superiormost two vasa brevia. The vessels are divided on the gastric side of the gastroepiploic vessels in order to avoid leaving an avascular greater omentum. Any posterior gastric adhesions are divided

6. *Freeing of the Lesser Curvature.*—The entire lesser curvature is freed by serial division and ligation of the gastrohepatic omentum. The left gastric

Fig. 6.—Techniques of Billroth I. Anastomosis completed.

vessels are divided close to their origin and doubly ligated with 0 black silk. At this point added exposure may occasionally be achieved by dividing the triangular ligament of the left lobe of the liver and retracting the latter to the right.

7. *Division of the Anterior Vagal Fibers.*—One to two inches of added mobility of the stomach may be had by severing the anterior vagal fibers on the abdominal portion of the esophagus. The proximal end of these fibers should be ligated to avoid troublesome bleeding. This maneuver is purely a mechanical expedient, and no physiologic effect is sought (Fig. 4, *d*).

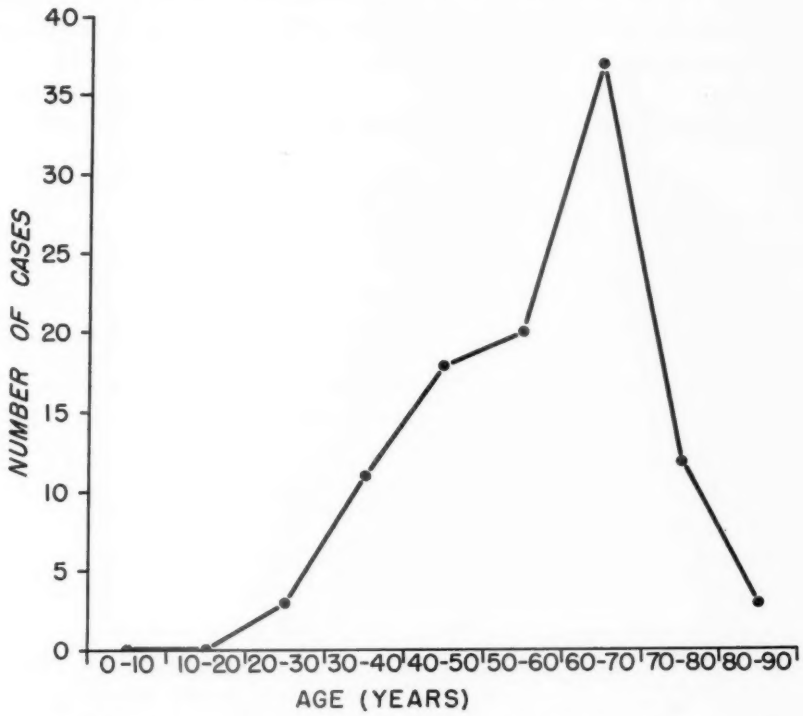

Fig. 7.—Age incidence in Billroth I series: January 1, 1948 to Dec. 31, 1951. Well over half of the patients are between the ages of 50 and 84 years.

8. *Resection of the Stomach and Closure of the Schoemaker Lesser Curvature Excision Line.*—The entire stomach should now be visualized so that approximately 75 per cent, or whatever amount is desired, may be resected. A Payr clamp is placed on the greater curvature portion of the stomach at the elected site of division for a distance of 5 cm. across the width. This portion of the stomach is divided. The Von Petz clamp is then angled up to the lesser curvature side of the esophagogastric junction from the tip of the Payr clamp, and a double row of Von Petz clips is placed along this line. The remainder of the stomach is divided between the clips, thus excising the entire lesser curvature after the method of Schoemaker[25] (Fig. 5, *a*). Measurement of the remaining stump of the stomach by the pattern method to be described later is done at this stage. The clip-closure of the Schoemaker line is reinforced with a single row of interrupted black silk inverting sutures.

9. *Anastomosis.*—If the end of the duodenum is suitable, an end-to-end gastroduodenostomy is performed. If the end is unsuitable (usually because of

a posterior penetrating ulcer), then a Nissen[19] type of closure of the end of the duodenum is used, and a terminolateral gastroduodenostomy is done, as described by Von Haberer, in 1922,[28] and Finney, in 1924.[11] In either instance an open, two-layer interrupted silk anastomosis is performed. The "critical angle" is now reinforced with a Finsterer[12] stitch. (Figs. 5, *b* and *c*, and 6, *a*, *b*, and *c*.) Again we wish to emphasize that the anastomosis should not be forced. If it cannot satisfy the generally accepted tenets of good surgical technique, a gastrojejunostomy should be done.

10. *Wound Closure.*—Interrupted No. 30 stainless steel wire buried sutures are placed in the linea alba and interrupted 0000 black silk is used to approximate the skin.

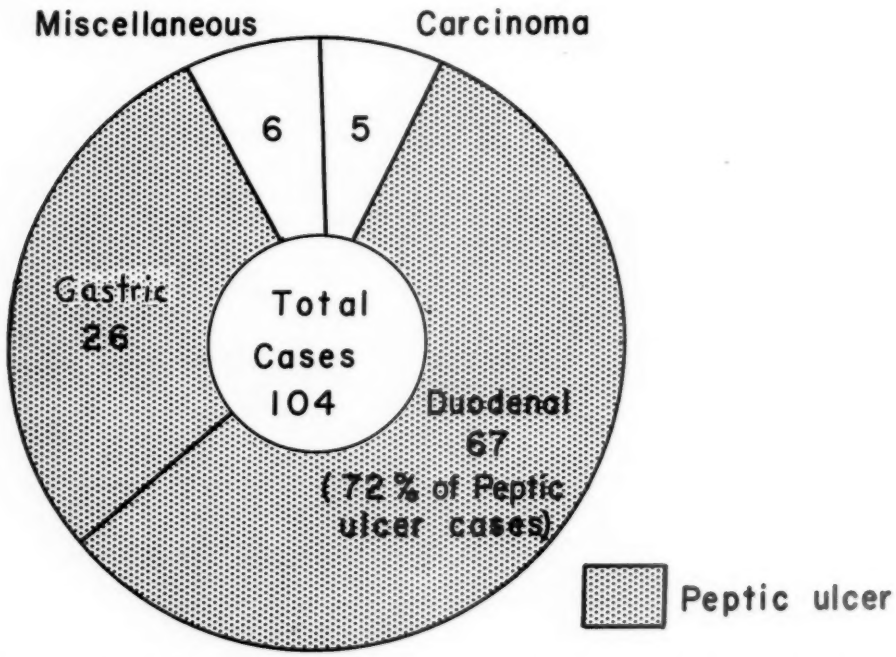

Fig. 8.—Billroth I series: Jan. 1, 1948 to Dec. 31, 1951. Diagram shows the relative proportion of 104 cases with peptic ulcer (duodenal and gastric), those with carcinoma, and a miscellaneous group which is analyzed in Table V. It is noteworthy that 72 per cent of the ulcer cases had duodenal pathology.

ANALYSIS OF CASES

This series consists of 104 cases of Billroth I partial or subtotal gastric resection accumulated as previously described under "Selection of Cases."

Age.—Over half of our cases are between the ages of 50 and 84 years, a reflection of the fact that the greater part of the series is drawn from a county hospital (Table I and Fig. 7).

TABLE I. AGE INCIDENCE

Youngest patient (male)	22 years
Oldest patient (female)	84 years
Average age (male)	56 years
Average age (female)	58 years
Average age (both sexes)	57 years

Sex.—The predominance of men in this series (77 per cent as shown in Table II) reflects the usual sex incidence seen in other series.

TABLE II. SEX INCIDENCE

SEX	NUMBER OF PATIENTS	PERCENTAGE
Male	80	77
Female	24	23
Total	104	100

Race.—There are 101 white patients, 2 Negro patients, and 1 Japanese patient in the series. This is not unusual when one considers the distribution of population at large in this area.

Duration of History Prior to Surgery.—Reference to Table III reveals a wide range of duration of symptoms prior to surgery.

TABLE III. DURATION OF HISTORY

Average duration (90 cases)	7 years
Duration (14 cases)	Unknown
Range (90 cases)	0 to 30 years

Frequency of Indications for Surgery.—The four most frequently found indications for operation in this series are bleeding, presence of gastric ulcer, previous perforation, and obstruction of the stomach (Table IV). It is worthy of note that several of the indications found in Table IV often occurred together in the same patient. Five patients in the series had resections at the time of acute perforation. It is interesting to note that one patient had had a previous Billroth II with an inadequate resection and a marginal ulcer. In 12.5 per cent of the cases alcoholism interfered with the maintenance of a satisfactory medical ulcer regime, and we considered this a strong indication for surgery. One unusual indication was found in an extremely obese young woman who found that the diet necessary to control her ulcer symptoms caused her to gain weight.

Pathology.—Reference is made to Table V and Fig. 8. They are self-explanatory.

TABLE IV. FREQUENCY OF INDICATIONS FOR SURGERY

INDICATION	NUMBER OF TIMES PRESENT	PERCENTAGE OF CASES WITH INDICATION
Bleeding	46	44.2
Gastric ulcer	30	28.2
One or more previous perforations	29	27.9
Obstruction	21	20.2
Alcoholism	13	12.5
Perforation present	5	4.8
Carcinoma	5	4.8
Intractability	4	3.8
Gastric polypi	3	2.9
Hypertrophy of pylorus	1	1.0
Increasing obesity on ulcer diet	1	1.0
Stomal ulcer (previous inadequate Billroth II)	1	1.0
Incidental finding of ulcer at exploration for cholelithiasis	1	1.0

TABLE V. PATHOLOGY

PATHOLOGY	NUMBER OF CASES	PERCENTAGE OF ULCER CASES
A. Active ulcer or ulcer scar	93	100
1. Gastric	26	28
2. Duodenal	57	61
a. Acute perforation	5	72 per cent
3. Mixed (gastric and duodenal)	10	11
B. Carcinoma	5	
C. Hypertrophy of pylorus	2	
D. Gastric polypi and leiomyomata	1	
E. Postgastritic pseudopolypi	1	
F. No pathology found	2	
Total	104	

Extent of Resection.—In this series we have used four criteria for extent of resection: (1) surgeon's estimate of extent, (2) weight of the resected specimen, (3) measurements of the greater and lesser curvature lengths of the resected specimen, and (4) measurements by a new method, utilizing the polar planimeter which accurately measures the area circumscribed by the margins of patterns of the resected stomach as well as the residual stomach, made at the time of surgery (Fig. 9). We have found that Cottonoid is a suitable material for making these patterns.

It should be apparent that any method of measurement of extent of resection which does not take into consideration the amount of residual stomach is

TABLE VI. COMPARISON OF SURGEON'S ESTIMATE AND MEASUREMENTS USING PLANIMETER

PATHOLOGY	SURGEON'S ESTIMATE (PER CENT)	MEASUREMENTS WITH PLANIMETER	
		PER CENT RESECTED	SQ. CM. RESECTED
1 Duodenal ulcer	80	80	492
2 Early carcinoma	60	63	203
3 Duodenal ulcer	75	81	529
4 Duodenal ulcer	75	79	579
5 Duodenal ulcer	75	78	335
6 Gastric ulcer	65	70	404
7 Gastric ulcer	75	76	316
8 Gastric ulcer	65	45	258
9 Gastric ulcer	75	73	351
10 Gastric ulcer	75	74	262
11 Gastric ulcer	75	84	351
12 Duodenal ulcer	75	79	351
13 Duodenal ulcer	75	70	381
14 Duodenal ulcer	75	76	395
15 Gastric ulcer	60	67	459
16 Duodenal ulcer	80	84	375
17 Duodenal ulcer	58	68	496
18 Duodenal ulcer	68	69	329
19 Duodenal ulcer	75	72	339
20 Duodenal ulcer	73	78	412
21 Duodenal ulcer	66	69	392
22 Duodenal ulcer	80	80	396
23 Gastric ulcer	54	52	253
24 Duodenal ulcer	64	69	464
25 Gastric ulcer	65	70	324
26 Duodenal ulcer	82	79	441
27 Duodenal ulcer	—	73	367
Averages	70.9	72.5	379.8

unreliable. The reason for this is the marked variation in the degree of hypertrophy, dilatation, edema, and pathology among different resected specimens. Because of this, we feel that the surgeon's estimate and the planimeter measurements are most reliable. We found that after measuring the patterns of some of our resections with the planimeter and comparing these measurements with our estimates that we were soon able to estimate extent of resection fairly accurately. Table VI shows the close parallel between these figures in most of 26 cases.

Table VII shows the average values for each of the four criteria for each group of cases according to the pathology for which the surgery was performed.

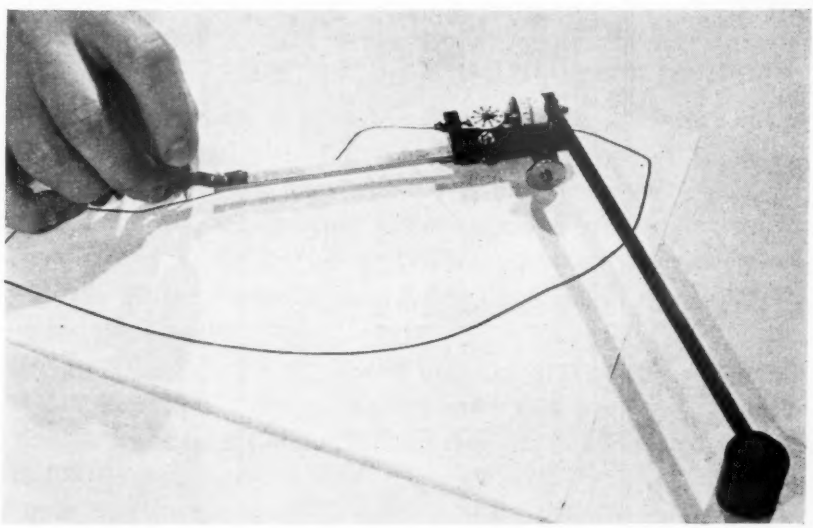

Fig. 9.—The polar planimeter is used to measure the areas of the resected specimen as well as the residual stomach.

Postoperative Complications.—The average length of stay in the hospital following operation in this series was 11 days, excluding the 2 deaths. Two other patients were also excluded in obtaining this average: one stayed 21 days awaiting a nursing home placement and another stayed in an Army hospital for over 43 days with a draining wound because of lack of fitness for full duty.

Table VIII contains a list of the postoperative complications encountered in this series in the order of frequency of occurrence. The relatively high incidence (11.5 per cent) of postoperative pulmonary complications is not surprising in a series containing so many individuals in the older age group. None of the three wound infections were of a serious nature. Each case of postoperative intestinal obstruction was due to old adhesions from previous surgery; 1 case necessitated re-exploration and the other responded to conservative management. There were 2 cases of mild postoperative upper gastrointestinal bleeding; both responded to conservative measures. One of the patients showed a small outpouching on the lesser curvature on the barium-meal x-ray studies. This may have represented a small leak of the suture line; however, he responded well to conservative management.

TABLE VII. EXTENT OF RESECTION (AVERAGE VALUES)

PATHOLOGY	SURGEON'S ESTIMATE		WT. OF SPECIMENS*		LESSER CURVATURE		GREATER CURVATURE		PLANIMETER		
	NUMBER MEASURED	PERCENTAGE	NUMBER MEASURED	GRAMS	NUMBER MEASURED	CM.	NUMBER MEASURED	CM.	NUMBER MEASURED	SQ. CM. RESECTED	PER CENT RESECTED
Duodenal† or mixed ulcer	55	74.5	58	223	64	14.0	64	25.0	17	395	75.5
Gastric ulcer	19	68.8	23	202	22	13.6	22	21.5	9	331	68.0
Pseudopolypi	1	90.0	1	206	1	14.0	1	22.0			
Carcinoma	4	65.0	3	190	4	12.0	4	22.0	1	203	63.0
Leiomyomata and polypi					1	12.0	1	14.0			
No pathology found	1	75.0	2	160	2	15.0	2	23.0			

*Fat removed.

†In addition, there is one case of duodenal ulcer in which a previous vagotomy had been performed, and this resection intentionally consisted of only about 25 per cent (antrumectomy). This case is not included.

TABLE VIII. POSTOPERATIVE COMPLICATIONS

COMPLICATION	NUMBER OF CASES	PERCENTAGE
Atelectasis and/or bronchopneumonia	12	11.5
Wound infection	3	2.9
Mechanical intestinal obstruction (due to old adhesions)	2	1.9
Postoperative bleeding (mild gastrointestinal)	2	1.9
Urinary tract infection	2	1.9
Died in hospital	2	1.9
Cerebrovascular accident or myocardial infarct	1	0.9
Adynamic ileus	1	0.9
Epididymitis	1	0.9
Early partial stomal obstruction	1	0.9
Transfusion reaction	1	0.9
Total	28	26.5

There were 2 hospital deaths. One patient was a 77-year-old woman who died 21 days postoperatively of a myocardial infarct and bronchopneumonia. The other was a 70-year-old man who had a minimal resection for hypertrophy of the pylorus and at the same time a resection of a stricture of the lower esophagus. He died 44 hours postoperatively. Autopsy permission was refused.

The 1 case of early partial stomal obstruction lasted for only 3 days and cleared up spontaneously.

Follow-up Studies.—There were 2 hospital deaths (described under "Postoperative Complications") out of the 104 cases (1.9 per cent). Neither of these hospital deaths could be attributed to the fact that a Billroth I was done instead of a Billroth II.

The follow-up studies on these patients are admittedly short and incomplete, due largely to the fact that so many of our patients are undependable and cooperate with clinic visits only if they are having incapacitating symptoms. All follow-up studies were conducted by personal interview by one of us or by members of the resident staff who have been instructed personally by one of us in the obtaining of this information. We have procured some postoperative information on 92 of the 104 patients (88 per cent) (Table IX).

We have graded results as follows: "Excellent" means that in all respects the preoperative difficulties with reference to the stomach or duodenum are

TABLE IX. RESULTS

TIME (MONTHS)	POOR	SATISFACTORY	EXCELLENT	DUMPING	DUMPING LOST
< 1	2*	7	10	4	0
1 to 4	0	19	9	7	3
4 to 8	1†	10	6	6	2
8 to 12	1‡	7	7	7	0
12 to 18	0	2	4	0	1
18 to 24	0	2	0	1	0
24 to 36	0	5	0	3	0
Total	4	52	36	28	6

*Two hospital deaths.

†Severe dumping and pain. Postoperative gastrointestinal series shows a duodenal diverticulum.

‡Died 11 months postoperatively of persistent carcinoma.

absent and that there is no incapacitation from any cause related to the operation. "Satisfactory" means that all preoperative difficulties have been resolved and that there is some mild incapacitation due to the operation. "Poor" means anything worse than mild incapacitation.

On the basis of this grading system, we have 36 of the 92 patients followed (39.1 per cent) classified as excellent, 52 (56.5 per cent) as satisfactory, and 4 (4.4 per cent) as poor, the last group including the 2 hospital deaths previously described. There are 88 cases out of 92 followed (95.6 per cent) which are considered satisfactory or better at the last time seen, as indicated in Table IX.

The last two columns in Table IX show the number of patients with the "dumping syndrome," indicated on the basis of the longest follow-up time at which dumping was present and also, in 6 instances, the time at which dumping disappeared. In no instance did dumping begin later than 2 weeks postoperatively if it had not been present before. In compiling these data we have utilized the following definition of the "dumping syndrome": a positive history of sweating, unpleasant warmth, or subjective flushing, nausea, palpitation, or explosive diarrhea beginning during or within 15 minutes after eating and at least partially relieved by lying down. A case was considered to have dumping if any of these symptoms occurred *at any time* in the postoperative period regardless of persistence, degree of incapacitation, or consistent occurrence. We have data concerning dumping on 86 cases; 28 (32.6 per cent) of these had dumping using the strict criteria listed above. Six cases of this group have lost their dumping syndrome, leaving 22 cases out of 86 with persistent dumping (25.6 per cent) as far as our current follow-up goes.

There was 1 case mentioned under "Postoperative Complications" which may have had a leaking suture line which healed on conservative management. There is no other case in the series where a leaking suture line was suspected. There was 1 case described in the same section, which had temporary early stomal obstruction spontaneously relieved.

There has been no instance of known recurrent ulceration in this series. Three cases were re-explored because of roentgenologic and endoscopic suggestion of lesser curvature gastric ulceration, but all three explorations failed to disclose any evidence of ulcer. (One of these three explorations was done primarily to remove a calculous gall bladder overlooked at the time of the first operation.)

DISCUSSION

The objective of any surgical operation is to correct the existing pathology with minimal disturbance of normal physiologic mechanisms. There are several known physiologic mechanisms which are dependent on the continuity of the stomach with the duodenum. Foremost among these is the stimulation of flow of bile and pancreatic juice by the presence of food in the duodenum. The shunting of the pathway of food away from the duodenum by gastrojejunal anastomosis interferes not only with the stimulation of flow of these important digestive juices, but also with the adequate mixing of them with food.[5, 7, 29, 30]

Wollaeger[30] has related part of the disturbed gastrointestinal function following subtotal gastric resection to the loss of fat and nitrogen in the feces. He showed that patients with a Billroth I lost significantly less than those with a Billroth II.

Bohmansson[3] reported a series of subtotal resections and found that 6 per cent of 104 cases of Billroth I had "intestinal disturbances" and that 24 per cent of 67 cases of Billroth II had such trouble.

Polya,[22] after whom is named one of the most popular modifications of the Billroth II, stated in 1940 that he preferred the Billroth I whenever possible because it came "nearer meeting the physiological standard."

There is experimental evidence to indicate that the presence of acid in the duodenum exerts an inhibiting effect on the secretion of acid by the stomach.[6, 21, 24, 26] Dragstedt, Oberhelman, and Smith[8] were able to show, in the dog, that antral hyperfunction resulting from its transposition into the colon produced stomal ulcer in 80 per cent of gastrojejunal anastomoses and in only 20 per cent of gastroduodenal anastomoses. Therefore, the factor of duodenal inhibition of gastric secretion may be an insurance factor against stomal ulcer when gastroduodenal anastomosis is used.

Further protection against stomal ulceration in gastroduodenostomy is due to the fact that the duodenal mucosa is more resistant to acid-pepsin digestion than is the jejunal mucosa.[5, 14, 15] In addition, this places the stoma nearest to the neutralizing alkaline juices.

There are certain technical advantages of the Billroth I in addition to the physiologic aspects described above: (1) as emphasized by Clagett and Waugh,[5] and Priestley,[23] it is faster and easier. (2) Blowout of the duodenal stump is avoided. In the case of the end-to-end anastomosis there is no stump closure; when the terminolateral anastomosis is used, the proximity of the stoma affords adequate decompression of the duodenal lumen if necessary.[9, 10] (3) The entire operation is performed in the supramesocolic compartment of the abdomen with minimal disturbance of the colon and mesocolon.[5, 10, 22] (4) Kinking at the stoma is avoided.[10]

Leakage of the suture line at the "critical angle" should not be more prone to occur with gastroduodenostomy than it should with the Hofmeister-Polya anastomosis. In our series we had only one patient who might have had a local leak, and if it was present it was not serious and required no special treatment.

As noted previously, stomal obstruction was not observed to a serious degree in any of our cases.

Our measurements of extent of resection indicate that it is feasible to resect a sufficient amount of stomach according to the Billroth I method. As measured by the planimeter, we averaged approximately a three-fourths resection for duodenal ulcer and slightly less for gastric ulcer. If it is possible to perform an esophagoduodenostomy after total gastrectomy, it certainly is possible to utilize the duodenum after a subtotal resection.

Most surgeons hesitate to use the Billroth I in cases with duodenal pathology.[5, 13] However, Fallis and Barron[10] reported a series of 50 cases in which they used the end-to-side anastomosis; 42 of them had duodenal pathology.

Seventy-two per cent of our peptic ulcer cases had duodenal pathology. Since we have been using the end-to-side anastomosis in cases unsuitable for the end-to-end gastroduodenostomy we have been able to use the Billroth I in 88 per cent of cases with duodenal pathology. The other 12 per cent were done by other surgeons who did not have preference for the Billroth I.

The total incidence of dumping in our series is 32.6 per cent, and 25.6 per cent have persistent dumping for the length of time followed and by the strict criteria of dumping which we use. Only one patient is considered to have severe dumping. Preliminary tabulation of follow-up on a series of Billroth II's at the King County Hospital, Seattle, for the same period of time as our series indicates that about 40 per cent of those followed have dumping, by the same criteria which we use in this series.

Reports of dumping in the literature show an incidence ranging from 0 per cent[10] to 75 per cent.[18] Perman[20] found a lower incidence in the Billroth I group than in the Billroth II group.

We are not prepared to claim any superiority of the Billroth I over the Billroth II as far as dumping is concerned.

To summarize, we feel that there are distinct advantages of the Billroth I over the Billroth II and that the principal criticisms against the procedure are for the most part unjustified on the basis of our own experiences and those of others. The advantages, we feel, not only justify, but indicate, the more widespread use of this procedure.

SUMMARY AND CONCLUSIONS

1. A series of 104 Billroth I gastric resections is presented.
2. An evaluation of the advantages and disadvantages is made.
3. The operative technique which we prefer is described.
4. The applicability of the Billroth I procedure to cases with duodenal pathology is stressed.
5. The Billroth I operation has certain advantages over the Billroth II procedure and should and can be used more extensively than it is at present.

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(See Discussion on page 434)

THE TREATMENT OF PEPTIC ULCERATION BY EXTENSIVE PARTIAL GASTRECTOMY WITH GASTRODUODENOSTOMY

A Preliminary Report

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INTRODUCTION

DESPITE the enthusiasm which followed the reintroduction of vagotomy in the treatment of peptic ulceration, extensive partial gastrectomy is still the method of choice in most clinics for the treatment of severe and intractable ulcers of the duodenum and in all clinics for the treatment of ulcers located in the stomach. The previously formidable mortality that accompanied partial gastrectomy has dropped to the neighborhood of 3 per cent, with several sizable series reporting even more favorable mortality rates.[1, 2] The mortality rates do not tell the whole story. Between 10 and 15 per cent of patients have unsatisfactory results because of functional and economic sequelae of varying degrees of severity.[3, 4] These sequelae include "dumping," diarrhea, reduced stomach capacity, inability to maintain proper weight and nutrition, reduced working capacity and, in some few cases, complete incapacity because of one or more of these unfavorable side effects.

Throughout the years there have been many gastric resections carried out with reconstruction of the intestinal tract by gastroduodenostomy, since Billroth[5] carried out his first resection (for carcinoma) by this method.† Usually, at least in this country, these procedures have been done for gastric lesions, the largest series having been reported from the Mayo Clinic.[6, 7] The principle, however, has been widely used on the continent, especially by the Schoemakers,[8, 9] for duodenal lesions, and, in this country, Fallis[10] has reported a series of such resections combined with vagotomy. Interest in this procedure has persisted because of general agreement that unfavorable postgastrectomy symptoms are greatly reduced in comparison to the number of such symptoms encountered after the more frequently employed resection with gastrojejunostomy. Indeed, this feeling is so strong that there have been sporadic attempts to overcome particularly severe postgastrectomy symptoms by taking down an existing gastrojejunostomy and effecting a gastroduodenal anastomosis.[11-13]

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†We have avoided the term "Billroth I procedure" as it automatically suggest to most surgeons that a limited resection was performed.

In the follow-up of patients from the all-male ulcer clinic at the Veterans Administration Hospital, West Roxbury, it has been established that significant numbers of poor functional and economic results were being observed following surgery. Warren and Meadows[4] reported an earlier series of cases from this clinic and listed considerable numbers of undesirable side effects. They found a larger percentage of poor results in the group that had surgery for gastric

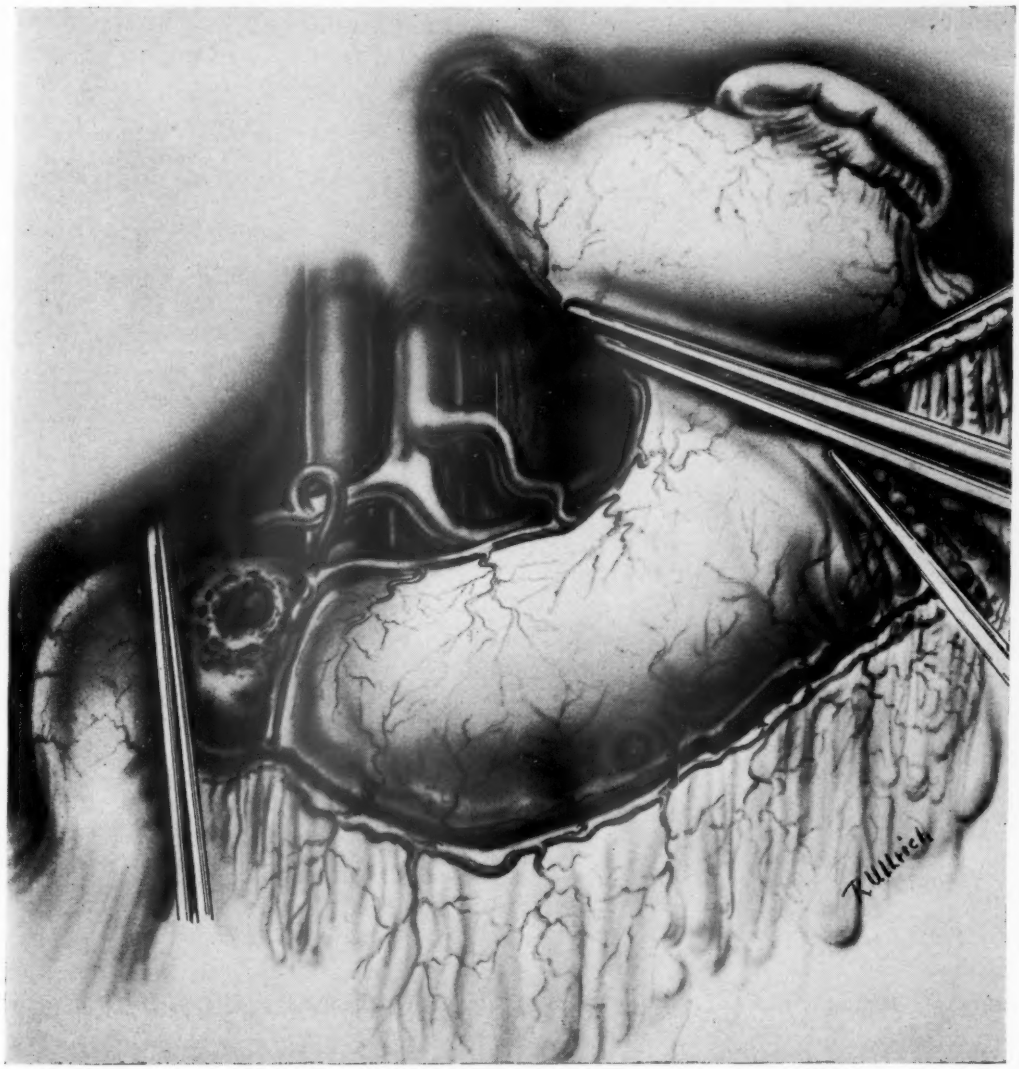

Fig. 1.—Partial gastrectomy with gastroduodenostomy, showing method and extent of resection.

ulcer. As will be shown, this trend has continued and is in sharp contrast to the general impression that gastric ulcer patients fare better as a group after surgery is performed than do those suffering from duodenal ulcer.[14, 15]

In view of this background of historical and local events, early in 1949 a program of resection with gastroduodenostomy was begun in this hospital in an effort to see whether the over-all results of surgery for benign peptic ulceration

could be improved. The ensuing account of this experience can be considered only a preliminary report since just three years have elapsed since the first case was done. The early cases were mostly for gastric ulcer and it was not until experience and confidence were gained that any appreciable number of duodenal ulcer patients were treated by this type of operation.

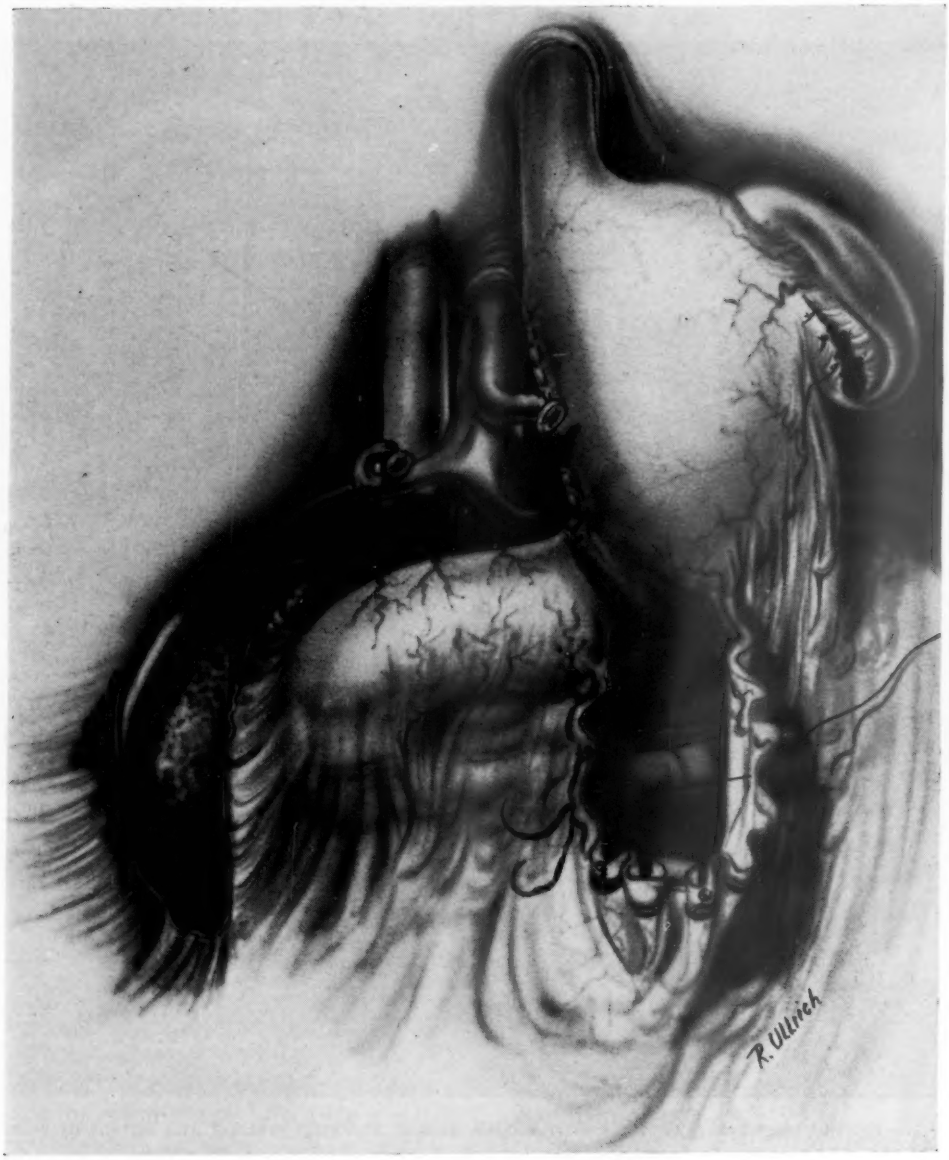

Fig. 2.—Partial gastrectomy with gastroduodenostomy. The completed anastomosis.

METHODS

The criteria for adequate partial gastric resection were rigidly followed.[2] These are: (1) the removal of essentially all of the lesser curvature, (2) the removal of at least three-fifths of the greater curvature, and (3) the removal

of all the antrum and pylorus with pathologic proof that a complete ring of duodenum, no matter how narrow, has been removed. Figs. 1 and 2 show the artist's conception of this procedure. The two important steps in securing adequate mobilization for anastomosis without tension are first, division of the tissues that run upward and to the left from the greater curvature to the spleen, including at least the lowest short gastric vessels, and second, division of the peritoneal reflection to the right of the duodenum so that extra mobility of the duodenum toward the left is obtained. An adequate resection was first performed in all cases and if it was then obvious that there would be undue tension because of obesity or difficulties in mobilization of the tissues, gastroduodenostomy was abandoned in favor of gastrojejunostomy. The angle along the lesser curvature

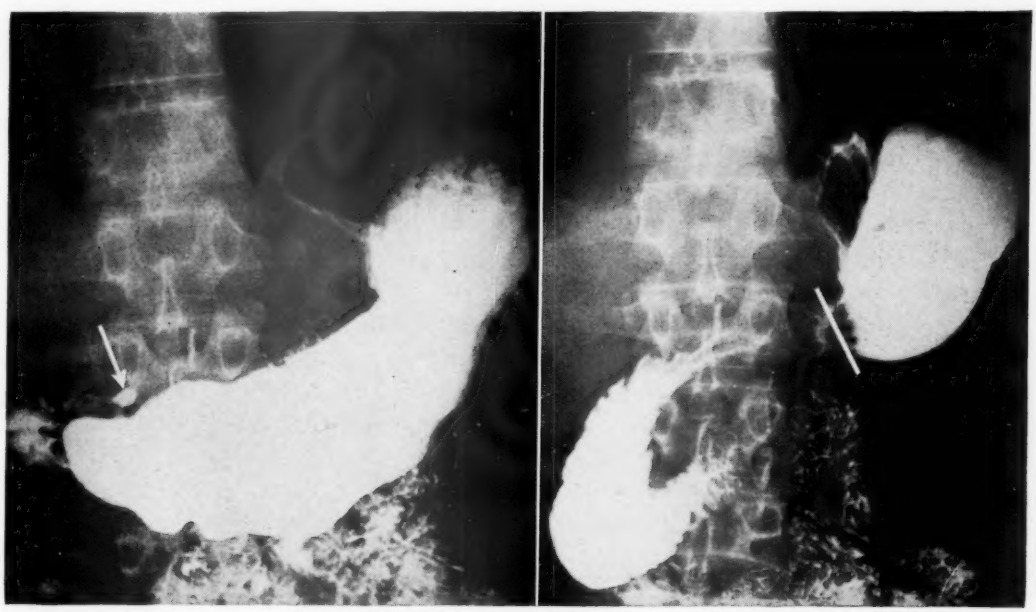

Fig. 2.—Preoperative and postoperative x-ray studies of duodenal ulcer patient who underwent resection with gastroduodenostomy. The arrow points to the ulcer crater in the preoperative film. The white line in the postoperative film indicates the site of the gastroduodenal anastomosis.

was closed, converting the stomach remnant into a tube, and end-to-end anastomosis was performed between the portion of the cut stomach nearest the greater curvature and the open end of the duodenum. In two cases the duodenal stump was closed and an end-to-side anastomosis carried out at the second portion of the duodenum. This alternate procedure seemed less desirable because it left a blind duodenal stump which is the major source of operative complications and mortality. The immediate advantages of end-to-end gastroduodenostomy are the absence of such a blind stump, and the absence of an afferent jejunal loop which may undergo temporary obstruction. In only one case undergoing gastroduodenostomy was there even slight evidence of peritonitis, whereas in the control group with gastrojejunostomy there was evidence of peritonitis, intraperitoneal abscess and/or fistula formation in five patients, with a fatal outcome in one instance.

Fig. 3 shows the pre- and postoperative x-ray examination of a duodenal ulcer patient who underwent resection with gastroduodenostomy. The postoperative film shows that at least two-thirds, probably three-fourths, of the stomach has been removed. The stomach remnant is rotated down and medially, and the anastomosis ends up well to the left of the midline—a routine finding in these patients.

MATERIAL

Table I shows the number of patients involved in this study. It includes all of the gastroduodenostomy operations, excluding cancer operations, performed until July, 1951. Each of the four groups represents a consecutive series ending in July, 1951, but the start of each series varies somewhat. The procedure of gastroduodenostomy seemed so well adapted to patients with gastric ulcer and normal duodenal tissues that it rapidly became the procedure of choice in this group. It was, therefore, necessary to reach back to July, 1948, in the gastric ulcer files to obtain controls who had resection with gastrojejunostomy, which explains the longer follow-up period in this group. On the other hand, in the duodenal ulcer group only a few gastroduodenostomies were done in the first year, and even as familiarity with the problems of effecting this procedure in the face of duodenal ulceration increased it could never be performed in as many as half of the cases because of inadequate duodenal tissues for safe anastomosis. Hence, in order to obtain a control group of duodenal ulcer patients with gastrojejunostomies having approximately the same average follow-up, it was necessary to go back only to January, 1950. In both gastroduodenostomy groups the series started in January, 1949.

TABLE I. EXTENSIVE PARTIAL GASTRECTOMY FOR BENIGN ULCER (163 PATIENTS*)

	PATIENTS	HOSPITAL DEATH	LOST	FOLLOWED	AVERAGE FOLLOW-UP (MONTHS)
I. Duodenal ulcer					
A. Gastroduodenostomy	39	0	2	37	13
B. Gastrojejunostomy	74	1	1	72	12
II. Gastric ulcer					
A. Gastroduodenostomy	30	0	2	28	16
B. Gastrojejunostomy	20	0	1	19	24
Total	163	1	6	156	
Per cent of total		0.6	3.7	95.7	

*Consecutive cases in each of the four groups.

It will be immediately obvious that the control groups, at least in the duodenal ulcer patients, are not ideal, because in the latter part of the series the determining factor as to which type of operation was performed was the anatomic situation at operation. The larger the ulcer and the greater the amount of inflammation in and around the duodenum, the more likely the patient was to have gastrojejunostomy.

RESULTS

A. *Reduction of Acid Secretory Activity.*—Table II shows the reduction of acid secretory activity in volume, free acid, and total acid in all patients on

whom complete studies were carried out before and after resection with gastroduodenostomy. These figures show a satisfactory drop in secretory activity.[16] It may be that the figures are more significant than similar studies on patients who have had gastrojejunostomy because, even though the pyloric barrier has been removed in the gastroduodenostomy patient, there is probably less alkaline reflux into the stomach than there is following gastrojejunostomy.

TABLE II. ACID SECRETION AFTER HISTAMINE; EXTENSIVE PARTIAL GASTRECTOMY WITH GASTRODUODENOSTOMY

	PATIENTS	PREOP.	POSTOP.	REDUCTION (%)
I. Duodenal ulcer	19			
Av. vol./30 min. (in c.c.)		90	30	67
Av. free acid		53	20	62
Av. total meq./30 min.		4.8	0.6	87
II. Gastric ulcer	7			
Av. vol./30 min. (in c.c.)		38	28	26
Av. free acid		48	4	92
Av. total meq./30 min.		1.8	0.11	94

B. *Functional and Economic Results.*—Table III shows the late functional and economic complications comparing only the two types of operation, without regard to whether the original lesion was gastric or duodenal. The most striking features of this table are the complete lack of severe dumping in the gastroduodenostomy group and the relative lack of mild dumping and diarrhea. Even the two patients listed under mild dumping exhibited slight and atypical manifestations of this troublesome phenomenon. The "small stomach" phenomenon, which is the least crippling of the common postgastrectomy difficulties, is the only one in which gastroduodenostomy came off as badly as gastrojejunostomy. These people are quite well if they do not overeat even a spoonful or two beyond their known capacity. They usually have to take extra meals and, although they can hold their weight, they rarely gain. The figures regarding economic potentialities show an interesting trend, but the groups are too small to be of particular significance.

C. *Recurrent Ulceration.*—Table IV shows the recurrent or stomal ulcers observed. Since the follow-up time is short it is probable that further recurrences

TABLE III. LATE FUNCTIONAL AND ECONOMIC COMPLICATIONS OF RESECTION* (156 PATIENTS FOLLOWED)

	65 PATIENTS WITH GASTRODUODENOSTOMY		91 PATIENTS WITH GASTROJEJUNOSTOMY	
	NO.	PER CENT	NO.	PER CENT
Severe dumping	0	0	10	11
Mild dumping	2	3	14	15
Diarrhea	2	3	11	12
Small stomach	22	31	17	19
Inability to gain weight	15	23	18	20
Inability to hold weight	5	8	15	16
Reduced work capacity	6	9	12	13
Unable to work	2	3	10	11

*Since complications are often multiple when they occur, the total number of complications is far greater than the number of patients with complications.

will be seen in both groups. The earliest recurrence was evident in three months, the latest in thirty months, after operation. All of the recurrences occurred in the group undergoing gastroduodenostomy. It is possible that the one recurrence after surgery for gastric ulcer should be in the duodenal group. This patient had had typical recurrent ulcer symptoms for ten years, and was shown to have high acid secretion. He developed somewhat different symptoms prior to surgery and displayed a high and acute gastric lesion at operation with no evidence of duodenal ulcer at that time.

TABLE IV. RECURRENT ULCERS
(156 PATIENTS FOLLOWED)

	PATIENTS	RECURRENCES	PER CENT RECURRENCES
I. Gastroduodenostomy	65	5	7.7
A. Duodenal ulcer	37	4	10.8
B. Gastric ulcer	28	1	3.6
II. Gastrojejunostomy	91	0	0

Without attempting to minimize the serious import of these recurrences, we consider them all so far to have been mild. No patient has come to reoperation, only one has been rehospitalized. Four have shown complete healing, by x-ray evidence, after dietary treatment. All are regularly employed, and all but one are much happier than they were before surgery. Nevertheless, they have had definite recurrences and must be classified as complete failures of the method, although four of them would dispute this statement. Continued observations in this group will be of great interest.

TABLE V. RESULTS OF RESECTION
(157 PATIENTS)*

	PATIENTS	SATISFACTORY		UNSATISFACTORY	
		NO.	PER CENT	NO.	PER CENT
I. Gastroduodenostomy					
Duodenal ulcer	37	32	86.5	5	13.5
Gastric ulcer	28	25	89.0	3	11.0
Total	65	57	87.7	8	12.3
II. Gastrojejunostomy					
Duodenal ulcer	73	63	86.3	10	13.7
Gastric ulcer	19	11	57.9	8	42.1
Total	92	74	80.4	18	19.6
Grand total	157	131	83.4	26	16.6

*One hundred fifty-six patients followed plus one hospital death.

D. *Over-all Results.*—Table V records the over-all results. The satisfactory results[17, 18] are those patients completely free of medical care, working regularly. They are physically and economically solvent, although about half of them have some minor difficulty such as minimal dumping, necessity of avoiding certain foods, or inability to gain the weight they would like. The unsatisfactory results are those patients who still require medical care. Their problems range from troublesome dumping and strict dietary programs, through reduced or absent working capacity, to recurrent ulceration, and, of course, the single death. The

previously mentioned trend for gastric ulcer patients with gastrojejunal anastomosis to do poorly has continued. The increased percentage of unsatisfactory results after gastrojejunostomy (19.6) is suggestive, but not statistically significant, as compared to that after gastroduodenostomy (12.3).

SUMMARY

A series of patients undergoing surgery for benign peptic ulcerations treated by extensive partial gastric resection with gastroduodenostomy has been presented. This procedure is safe and feasible in nearly all cases of gastric ulcer requiring surgery, and in somewhat less than half of all cases of duodenal ulcer requiring surgery.

When compared to a series of patients whose resections were accompanied by gastrojejunostomy, patients with gastroduodenostomy had fewer serious operative complications and no mortality.

After operation with gastroduodenostomy the functional and economic results were better than in patients who had gastrojejunostomy. This was particularly true in patients with gastric ulcers. The most striking difference was the almost complete absence of the dumping phenomenon.

Offsetting the good functional and economic results in the group undergoing gastroduodenostomy was the fact that all the recurrent ulcers observed fell in this group.

CONCLUSIONS

1. In the treatment of benign peptic ulcers, resection with gastroduodenostomy can be effected without compromising on the amount of stomach removed. There are fewer functional and economic difficulties after this operation than after the commoner resection with gastrojejunostomy.

2. This procedure is the operation of choice in patients with gastric ulcer.

3. Because of the increased tendency to recurrent ulceration, this procedure cannot be recommended for patients with duodenal ulcer requiring surgery. It has enough promising features, however, that further studies and observations are warranted.

ADDENDUM

Since the paper was read, there have been two more definite stomal ulcers plus one probable one in duodenal ulcer patients who were subjected to resection with gastroduodenostomy. In addition to this, one of the patients mentioned in the text as having a mild and easily controlled recurrence has developed severe symptoms and has been rehospitalized. There are still no known recurrences in the group undergoing resection with gastrojejunostomy.

Resection with gastroduodenostomy has been completely abandoned in this clinic for patients with duodenal ulcers. It is still being used for patients who have benign gastric ulcers.

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DISCUSSION

DR. KEITH S. GRIMSON.—Our chairman, Dr. Ravitch, has just commented that this discussion of reports on subtotal gastric resection could be considered a threat. Instead, the intention is to congratulate the authors of each paper on their careful study, conservative interpretation of results, and low mortality rate. Reduction of mortality rate of resection is important; it is in respect to safety that vagotomy and gastroenterostomy has had its greatest advantage. The use of gastroduodenostomy as in the Billroth I resection or of a pyloroplasty technique following vagotomy minimizes physiological abnormality by maintaining direct continuity. Nevertheless, it would increase incidence of recurrence of ulcer if the lumen at the site of anastomosis narrows or contracts, and these techniques have not been popular. Decrease of incidence of the dumping syndrome, if achieved, would be welcome.

It is well for all of us carefully to examine, study, and report results of operations for ulcer, particularly long-term results. It is hoped that by study and by changes of method the small, but definite, incidence of poor results with any gastric operation will be decreased. Extensive or three-quarter gastric resection would reduce incidence of stoma ulcer, but might increase the number of patients with subnormal weight, dumping syndrome, anemia, etc. Perhaps the usual policy of one-half to two-thirds resection yields greater patient satisfaction. Stoma ulcers, when they occur, can now be readily treated without sacrificing more of the stomach. The comment about prediction of occurrence of the dumping syndrome in emotionally unstable patients was interesting. Comparison of statistics following any type of gastric surgery for ulcer will probably include in common a certain low percentage of gloomy results among individuals who, though relieved of ulcer, can never be rehabilitated.

All of us do resections, using one technique or another, at least for certain ulcer problems. It seems appropriate to suggest that all of us also use vagotomy and gastroenterostomy,

at least under certain circumstances. Mortality rate of resections, for example, can be reduced by using vagotomy and gastroenterostomy instead whenever the duodenum is extensively adherent or inflamed, or for stoma ulcer following previous resection or gastroenterostomy. Vagotomy and gastroenterostomy as a routine procedure for duodenal ulcer has yielded satisfactory results. Combined vagotomy and resection, however, would probably unnecessarily increase the number of subnormal patients.

DISCUSSION ON "A CRITICAL EVALUATION OF THE BILLROTH I GASTRIC RESECTION" BY DR. HORACE G. MOORE, JR., AND DR. HENRY N. HARKINS,* AND "THE TREATMENT OF PEPTIC ULCERATION BY EXTENSIVE PARTIAL GASTRECTOMY WITH GASTRODUODENOSTOMY" BY DR. FREDERICK P. ROSS AND DR. EDMUND C. MEADOWS

DR. STANLEY O. HOERR.—I have enjoyed the two papers very much and agree with the authors that the Billroth I procedure is probably the best operation for gastric ulcer. Perhaps, as Dr. Ross suggests, we should drop the term "Billroth I" and say end-to-end gastroduodenostomy. We have been employing gastroduodenostomy selectively on one service at the Cleveland Clinic for gastric ulcer and for sma'l gastric cancers lying very low. We have no experience with this operation for duodenal ulcer because, as some of you may know, at the Cleveland Clinic we believe that vagotomy with gastroenterostomy is preferred to gastric resection. The system that we follow is to leave the duodenal stump unclosed until the appropriate resection has been carried out. Then, if there is sufficient mobility of stomach and duodenum, an end-to-end gastroduodenostomy is carried out. Sometimes it is possible to do an esophagoduodenostomy after total gastric resection, but, in any event, the decision can be postponed until after the correct amount of stomach has been removed. It has also been our clinical impression that the dumping syndrome, although it does occur in the Billroth I, is less severe than with the gastrojejunostomy. I have one patient to report who was a great surprise to us in that a duodenal ulceration apparently developed at the stoma of a gastroduodenostomy after a gastric resection for gastric ulcer. The patient was an elderly gentleman with the low free acids characteristic of gastric ulcer. He remained symptom free after his gastroduodenostomy for about a year and then developed symptoms of recurrent ulcer. Roentgenograms suggested a duodenal ulceration. The symptoms responded to medical treatment and the x-ray appearance returned to normal.

DR. ROBERT ZOLLINGER.—I am sure we have all enjoyed this discussion very much. It has been a very honest evaluation of the Billroth I operation. The late Dr. Elliott Cutler was a great believer in this operation. As a matter of fact, most of his residents learned how to do this procedure before they felt safe to carry out a gastroenterostomy. I am perfectly sure, however, that we didn't take out enough of the stomach. Just before the war, I called in about two dozen patients, as I recall, for their five-year evaluation, and found that sometime during this period about half of these patients had shown evidence of recurrence. From that time on we felt a more radical resection of the Billroth II type was indicated; but in evaluating our results of the very radical resection of this type, we had to confess that we had too many economic, as well as dietary, cripples. Apparently the problem of the surgical treatment of ulcer is not yet well established since men 3,000 miles apart are talking about it. We have, therefore, gone back more recently to the Billroth I type of resection and have added vagotomy, believing that in view of our previous experience, everything possible must be done to lower the amount of acidity. I think, too, that a very thorough evaluation of the rehabilitation of the patient is very important. As Dr. Grimson pointed out, we should have at our command a variety of operations to give the patient the best possible care.

DR. LYLE HAY.—I have two observations. First, in the patients with small stomachs, on gastroscopy, we have been able to demonstrate that there has been poor function of the

*See page 408 for article by Moore and Harkins.

stoma, with either microstomia or some evidence of lack of the pseudopyloric action that you usually see. Second, I have converted two patients from the Billroth II to the Billroth I type of anastomosis for severe dumping syndromes. The follow-ups suggest that they are both going to be relieved of their symptoms. We have noted, however, that all of our patients with the Billroth II type of anastomosis who have had severe dumping syndrome have had a severe psychoneurosis and I suspect that that is one of the big factors in the dumping syndrome. I am not sure that the improvement of these two patients will continue over a long period of time.

DR. WILLIAM E. ABBOTT.—We have been interested in this problem for several years and, while we have done only about fifteen gastroduodenostomies following gastric resections, we have made a few observations that might be pertinent to this discussion. The first slide was made from roentgenograms taken preoperatively of an obese woman who had had recurrent bleeding episodes due to a duodenal ulcer. By comparing the size of the stomach with that remaining, as shown in the next slide, it is apparent that about four-fifths of the stomach was resected and a gastroduodenostomy was done.

I was wondering if the high frequency of the dumping syndrome seen by Dr. Moore and Dr. Harkins, which did not occur in the cases reported by Dr. Ross and Dr. Meadows, might not result from stasis in, and dilatation of, the duodenum produced by twisting it in the process of mobilization.

In several patients in whom we mobilized the duodenum, and the dumping syndrome occurred, barium seemed to churn about in the first and second portion of the duodenum which was dilated when fluoroscopy was performed. I believe the symptoms in these patients were due to the impaired drainage caused by rotating the duodenum.

Since we no longer mobilize the duodenum, the dumping syndrome has not been apparent, although we have been able to do a gastroduodenostomy in a high percentage of cases by cutting the gastrophrenic ligament and bringing the stomach down and over to the right side of the abdomen.

The first two slides, as well as the next two, show that the magenblase, or dome of the stomach, lies parallel and immediately below the diaphragm preoperatively, while postoperatively it has not only dropped from the diaphragm but faces the left side of the abdomen instead of facing cephalad.

Since the ulcerating lesion on the lesser curvature of the stomach in the third slide was thought to be a carcinoma, a radical resection of the stomach and surrounding tissues was performed. It can be seen that probably more than nine-tenths of the stomach was resected, and yet a gastroduodenostomy was feasible due to the fact that the stomach was mobilized.

In our experience, then, a very radical resection followed by a gastroduodenostomy is feasible in a great many instances if the stomach is mobilized by cutting the gastrophrenic ligament.

In viewing the anatomy of this region in a considerable number of autopsies, we are of the opinion that a gastroduodenostomy by this technique would be possible in almost every patient, regardless of the patient's build or the extent of obesity. (In patients where the ulcer was located several inches or more distal to the pylorus it might not be feasible or desirable to do such a procedure.)

We have been interested in the physiologic and nutritional aspects of gastroduodenostomy, as compared to gastrojejunostomy, following a resection, and hope to have some information along this line in the near future. It would seem as though a gastroduodenostomy would not only be a more physiologic operation but that the diarrhea and the inability to gain weight seen in some patients following a resection and gastrojejunostomy might be avoided.

I am especially interested in knowing how Dr. Moore and Dr. Ross feel about our observation on the dumping syndrome and the possibility that it could result from torsion of

the mobilized duodenum. Torsion might also account for stasis and distention of the jejunum resulting in at least one factor producing the dumping syndrome in patients following a gastrojejunostomy.

I have seen the dumping syndrome in two patients who had never had the stomach or duodenum operated on. In both patients, distention of the first part of the duodenum was apparent. In one case it was due to an ulcer scar, or postcholecystectomy injury of the duodenum, and in the other to partial obstruction at the ligament of Treitz. While stasis or partial obstruction might not be the only cause of the dumping syndrome, it may be an important and avoidable factor.

DR. HENRY N. HARKINS.—As far as the extent of gastric resection is concerned, I believe it to be a crucial point and, in my opinion, not enough attention has been paid in the past to recording quantitatively this factor. I will pass around a piece of the cottonoid that we use for cutting the patterns to measure the size of the stomach remnant. The method of measuring by x-ray, as used by Dr. Abbott and Dr. Holden's group, deserves consideration, and, with our method, is the only one that considers the size of the segment of stomach left behind as well as that removed. At the Mayo Clinic, a nomogram is used for the estimation of the extent of gastric resection. In using the nomogram, consideration is given to both the thickness of the muscularis at selected points and the weight of the segment removed. While this method is a quick one, at certain points on the scale a small difference in thickness of the muscularis will indicate a very large difference in the extent of resection. As far as Dr. Ross's excellent paper is concerned, his account compared the results of the two techniques (Billroth I and Billroth II), while in our paper we did not compare to any great extent, but merely reported the results of one technique (Billroth I). In one of his illustrations, it would seem that Dr. Ross does not do as extensive a duodenal mobilization as we do. Possibly that was the artist's interpretation rather than what the surgeon does. While this difference in extent of duodenal mobilization might explain the difference in incidence of dumping syndrome following the Billroth I in the two series, it seems more likely that the following factors may be more important: (1) difference in type of patient material (charity patients of older age group in our series), (2) difference in size of stoma, and (3) difference in criteria for dumping. One final point should be mentioned. If the name of Billroth is to be removed from the Billroth I operation because the modern procedure is now done more radically than in 1881 by Billroth, it would seem equally essential to eliminate the eponymic designation from all gastric operations (Polya, etc.), for they, too, are done with a greater percentage of stomach removal than when originally described.

DR. MOORE (Closing).—I want to thank the discussants of these two papers for their interesting comments. As far as dumping is concerned, which seems to be one of the most controversial points, we certainly do not know its cause. The literature is full of reports of dumping, varying from 0 per cent to 75 per cent incidence. Ours, of course, is somewhere in the middle. As far as being due to torsion of the duodenum, we can't say for certain that it is or that it is not. One thing to be brought up, though, is the fact that approximately the same percentage of our Billroth II cases, resection with gastrojejunostomy, which we have followed and which did not have mobilization of the duodenum, had dumping, using our criteria. I was very interested in Dr. Hay's remark that he had converted two Billroth II's to Billroth I's with at least initial benefit in dumping. Einar Perman reported a series of twenty-five cases of conversion of Billroth II to Billroth I with anywhere from complete to almost complete remission from dumping in twenty-four of the cases. I might also say with regard to Dr. Hoerr's remark that, although I neglected to mention it, we, too, leave our duodenal stump open until after we have performed what we consider to be an adequate resection. Again, I wish to thank the discussants of our paper.

DR. ROSS (Closing).—I think that Dr. Abbott may have put his finger right on the difference in the techniques of Dr. Harkin's group and ours, which may account for the striking difference in the amount of dumping observed in the follow-up of the two

groups. We have mobilized the duodenum only as much as necessary and have sought our greatest mobility on the side of the gastric remnant. I gather that your group, Dr. Moore, has gone all out to mobilize the duodenum much as though you were starting to resect it and the head of the pancreas. This is the principal divergence in our techniques and may account for the difference in our dumping statistics.

I certainly agree with Dr. Hay about the neuropsychiatric implications of the dumping problem. In our opinion, the greater the psychiatric overlay in a patient, the more likely he is to be plagued with dumping after his operation. In a few cases this influenced us to effect a resection with gastroduodenostomy in the face of rather marked technical problems, rather than fall back on gastrojejunostomy, because we were quite sure these unhappy individuals would exhibit dumping if we used the latter type of anastamosis, and almost certain they would not after gastroduodenostomy.

I would like to thank all the discussers.

Editorial

Halsted and the Society of University Surgeons

HAD William Stewart Halsted been permitted to attend the centenary celebration of his birth in Baltimore last February, no presentation would have thrilled him more than the papers recorded in this issue of SURGERY, given by members of the Society of University Surgeons. This society, composed of young surgeons who have completed the graduated university residency training in surgery, is indeed carrying on the Halsted tradition. The training program which they had was essentially the training program inaugurated by Dr. Halsted; in fact, the program which he initiated has probably not been improved upon by any other school. These young men are dedicating their lives to a career in academic work.

No greater tribute has been paid Dr. Halsted than the wide acceptance of his residency system for training surgeons. Adopted by him from the German plan, the residency system was designed to "produce not only surgeons but surgeons of the highest type, men who will stimulate the first youths of our country to study surgery and to devote their energies and their lives to raising the standards of surgical science." The Society of University Surgeons is made up of such men, and the papers to be found in this issue of SURGERY are samples of their investigative work.

Dr. Halsted would have been astounded at the surgical progress made since his death in 1922, especially in the development of intrathoracic surgery. The bold concept of Dr. Hardin and Dr. Schafer of replacing the aortic arch by means of an homologous graft would have been unthinkable in his day. Because of his special interest in surgery of the great blood vessels, he would have warmed to the papers of Dr. Gerbode, Dr. Dickinson, and Dr. Holman and of Dr. Wylie. He may well have dreamed at times that such work would be possible, and now it has come to fruition.

Nine of the twenty-three papers were, wholly or in part, concerned with experimental work in laboratory animals: the complete arterialization of the blood supply of the liver of dogs, total replacement of the aortic arch of dogs by homologous grafts, significance of the sympathetic nervous system in experimentally produced cholecystitis in the dog, autogenous transplantation of the thyroid in dogs, the effect of whole blood transfusions in experimental burns in dogs, the metabolism of cortisone in rats, extensive small bowel resection in young dogs, the regeneration of gastric mucosa in the dog, and the production of acute gastrointestinal ulcerations by lesions of the hypothalamus. These are but a few of the papers that were presented. Dr. Halsted's development of the Hunterian Laboratory at Johns Hopkins sponsored this approach to surgical

problems. It was he who had the insight to know that surgeons must have a laboratory which could serve as their workshop wherein problems of primary interest to the surgeon could be investigated. The many laboratories of surgical research in our medical schools throughout the country are, in reality, extensions of the Hunterian Laboratory which he founded. These laboratories are tangible proof of the surgeon's interest in the wider aspects of disease.

Other papers that were presented were concerned chiefly with clinical investigation of surgical problems: respiratory acidosis during anesthesia, cardiac catheterization studies of chronic constrictive pericarditis, controlled hypotension for surgical procedures produced by high spinal anesthesia, the effect of vagotomy on gastric physiology, the retention of plasma expanders within the circulation, the dangers of overloading the circulation with fluids given by hypodermoclysis, methods for determining the total body composition, congenital malformations of the rectum and anus, the pathology of megaloureters, the use of small intestinal segments for bladder substitutes, an evaluation of the Billroth I gastric resection, and the treatment of ulcer by extensive partial gastrectomy.

Dr. Halstead would have been pleased to have noted the youth of the men presenting these outstanding papers. A number of the senior authors are men still in their residency training. In a number of other instances the senior authors have only recently completed such residency training. The future of American surgery will remain bright as long as young men trained in the Halsted tradition continue to extend the borders of surgical knowledge. It was due to Dr. Halsted's foresight that residency training as we now have it in this country, at its best, was inaugurated. A by-product of this training is the Society of University Surgeons. They have set high standards for their organization from the beginning and they have maintained these standards.

—I. S. Ravdin, M.D.

Review of Recent Meetings

MEETING OF THE SOCIETY OF UNIVERSITY SURGEONS FEB. 7-9, 1952, BALTIMORE, MD.

F. A. SIMEONE, M.D., CLEVELAND, OHIO

THE fourteenth meeting of the Society of University Surgeons was held in Baltimore, Md., on Feb. 7, 8, and 9, 1952. As guests of the Johns Hopkins University, the Society had the great honor of participating in the University's celebration of the centennial of the birth of William S. Halsted. The meeting followed directly those of the Halsted Club and of the Society for Clinical Surgery.

The most memorable part of this meeting was the indescribable thrill of hearing first-hand the reminiscences about a master surgeon from his pupils and associates. The Society and its guests were literally spellbound by the addresses. The program of the morning meeting* (Dr. Emile Holman, Chairman) was as follows:

1. Welcome—President Detlev W. Bronk
2. Memories of Dr. Halsted—Dr. James Mitchell
3. Personal Recollections of Dr. Halsted—Dr. Samuel J. Crowe
4. My Experiences With Dr. Halsted—Dr. Willis D. Gatch
5. Personal Glimpses of Dr. Halsted—Dr. Arthur M. Shipley
6. A Pediatrician's Chance Recollections of Dr. Halsted—Dr. Edwards A. Park
7. Dr. Halsted as I Knew Him in the Hunterian Laboratory—Dr. F. L. Reichert
8. The Coming of Full Time to the Hopkins and Halsted's Attitude Toward the Plan—Dr. Alan M. Chesney
9. The Story of the Hunterian Laboratory—Dr. Warfield M. Firor
10. Comments on Halsted's Contributions to Arterial Surgery With Particular Reference to Progressive Occlusion of the Large Arteries by Means of the Aluminum Band—Dr. Emil Goetsch
11. The Impact of Halsted Upon Surgical Technique of Today With Particular Reference to His Operation for Hernia—Dr. William F. Rienhoff, Jr.
12. Dr. Halsted as an Anesthetist Knew Him—Miss Margaret Boise
13. The Story of Harvey Cushing's Appendix—Dr. Samuel C. Harvey
14. A Follow-up on the Jackstone Calculi Removed by Dr. Halsted—Dr. R. H. Follis, Jr.
15. The Fruition of Halsted's Concept of Surgical Training—Dr. B. Noland Carter
16. Halsted's Influence Upon British Surgery—Mr. David H. Patey, London
17. The Story of the Discovery of Nerve Block Anesthesia—Dr. Rudolph Matas (Presented by Dr. Holman)

In the afternoon, Dr. Mark M. Ravitch presented to the Society of University Surgeons a gavel made from parts of Halsted's teaching amphitheater preserved when the "New" Surgical Building was rased. The gavel was accepted for the Society by Dr. Harris B. Shumacker, Jr. The afternoon program continued with a presentation of papers by members of the Johns Hopkins University School of Medicine (Drs. Alfred Blalock and Harris B. Shumacker, Jr., Chairman).

1. Television Large-Screen Fluoroscopy and Radiography (Motion Picture)—Dr. Russell H. Morgan
2. Congenital Adrenal Hyperplasia: The Effect of Cortisone in Treatment and Its Differentiation From Virilizing Adrenocortical Tumors—Drs. L. Wilkins and L. I. Gardner
3. Experimental Cardiac Defects—Drs. Kay, Sabiston, Williams, and Blalock.
4. Physiological Considerations of Carotid Artery Ligations—Drs. A. Earl Walker and Herbert C. Johnson

*The papers presented at this session, and those by Drs. Leriche and Whipple presented at the Halsted Centennial Dinner, will be published in a special Halsted Centenary Issue of SURGERY, September, 1952.

5. Ligation of Hepatic Artery in Treatment of Bleeding Esophageal Varices—Dr. William F. Rienhoff, Jr.
6. Hemipelvectomy—Dr. Mark M. Ravitch
7. The Endocrine Management of Disseminated Prostatic Cancer Including Bilateral Adrenalectomy and Hypophysectomy—Dr. William Wallace Scott
8. Surgical Treatment of Aortic Septal Defects: Experimental and Clinical Experiences —Drs. H. W. Scott, Jr., and D. C. Sabiston, Jr.
9. Mitral Stenosis. Selection of Cases and Results of Surgical Treatment—Dr. E. C. Andrus

The Halsted Centennial Dinner was held in the evening and the speakers, Dr. René Leriche of Paris and Dr. A. O. Whipple of Princeton, described Halsted's contributions to surgery.

Papers by members of the Society were presented on the last two days of the meeting. They are published in this number of SURGERY. Dr. Francis D. Moore discussed "Concepts and Techniques in the Study of Total Body Composition and Its Changes After Trauma." This paper was not intended for publication *in toto* and is published below in abstract form.

Concepts and Techniques in the Study of Total Body Composition and Its Changes After Trauma, Francis D. Moore, M.D., Peter Bent Brigham Hospital, Boston, Mass.—(This work was carried out under a grant from the Atomic Energy Commission.) A firm understanding of the total body water in the normal human being is now based upon measurement in a large series of individuals using deuterium oxide dilution. As a result of our understanding in the normal individual, we are now able to approach measurements in patients with acute and chronic disease. Such measurements of total body water tell us not only how much water is in the body, but also the size of the "lean body mass" or that total fraction of body composition which is situated in relation to body water. The lean body mass is that portion of the body consisting mostly of skeletal muscle but including also the parenchymatous viscera and the blood stream, the fraction of the body actively engaged in energy exchange and transport of metabolites.

Knowing the total body water and the size of the lean body mass, we can, by difference (knowing the patient's total weight) calculate the amount of fat in the body. The total fat of the body may be considered as an anhydrous phase not involving water, even though its small extracellular phase does include a minor amount of lymph water measured, of course, in the deuterium dilutions.

The work of Pace and Behnke on interrelationship of fat, lean tissue, water, and body specific gravity has given us formulas for calculation of these interrelationships when any one variable is known. These formulas are applicable only in normal states or in patients who are "in equilibrium" with very slow-moving processes.

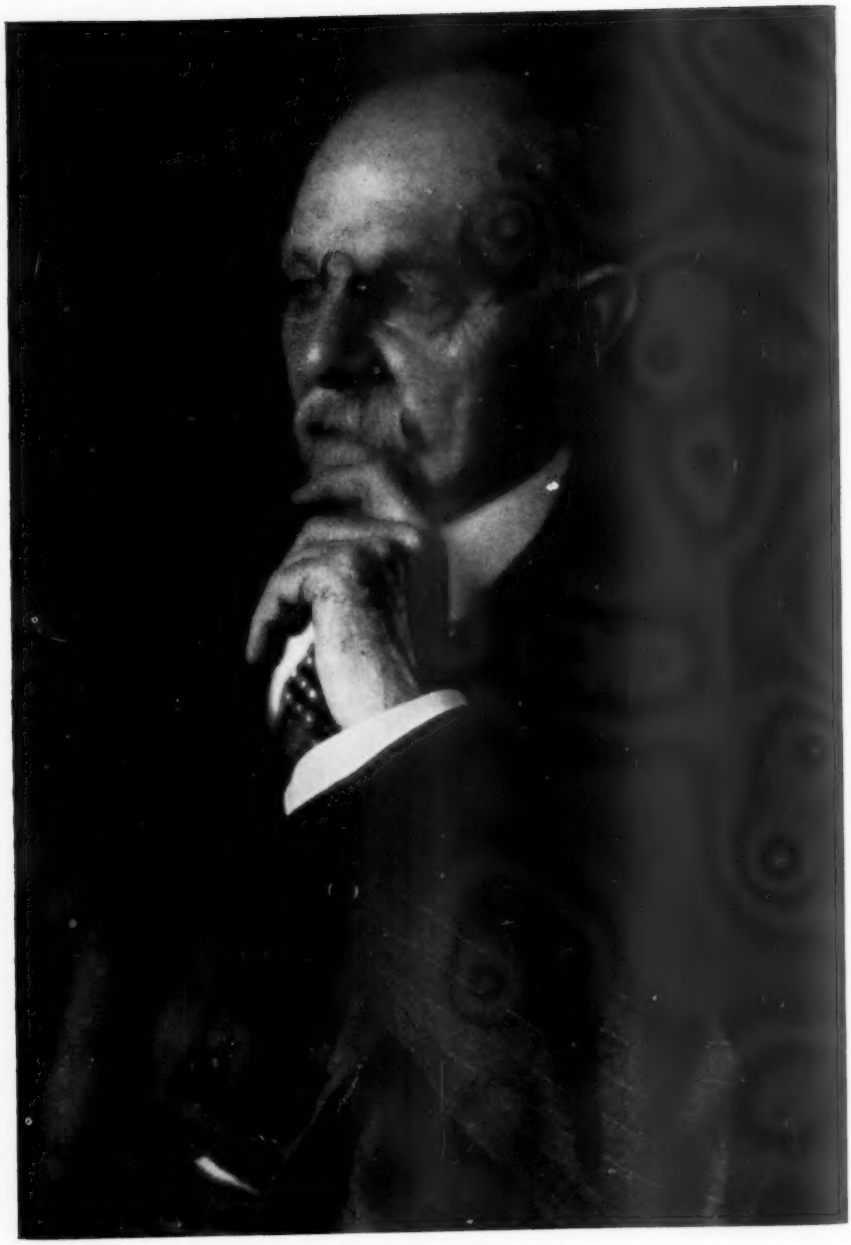
The measurement of the nitrogen balance is a direct measure of changes in lean tissue. About one-thirtieth of the weight of lean tissue is represented by nitrogen.

Thus, by measuring total body weight, total body water and nitrogen balance over a period of time, we can study the relative alterations in fat, fat-free solids, and water. We can also draw conclusions as to alterations in the state of hydration of lean tissue.

The greatest unknown variable in this type of calculation is the weight of wet skeleton, and changes which may occur in this fraction.

Employing these techniques, we have now studied thirty medical and surgical patients with acute and chronic disease. We find that fat oxidation is one of the common denominators of the postoperative metabolism, and that the final phase of convalescence constitutes the redeposition of fat. We find also that with very acute disease, massive operations, overwhelming infections, and high fever the rate of fat oxidation may be speeded up to the extreme rate of 600 Gm. per day. It is possible to calculate the contribution of endogenous fat calories to the metabolic requirements of the individual.

Observations on dehydration, overhydration and changes of hydration of lean tissue are also included in these studies.



William Stewart Halsted
(1852-1922)